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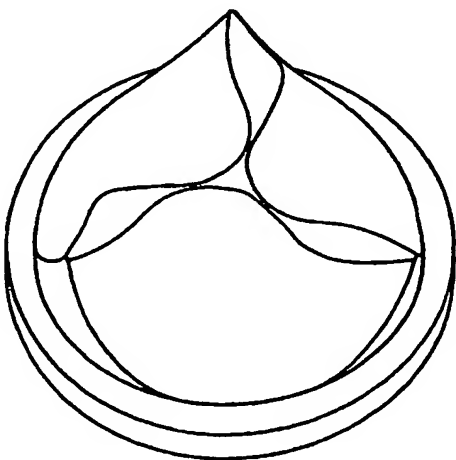
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(54) Title: **HEARTH VALVE PROSTHESIS AND METHOD OF MANUFACTURE**



(57) Abstract: The present invention provides a cardiac valve prosthesis comprising a frame and two or more leaflets (preferably three) attached to the frame. The leaflets are attached to the frame between posts, with a free edge which can seal the leaflets together when the valve is closed under back pressure. The leaflets are created in a mathematically defined shape allowing good wash-out of the whole leaflet orifice, including the area close to the frame posts, thereby relieving the problem of thrombus deposition under clinical implant conditions.

WO 01/41679 A1

1     **HEART VALVE PROSTHESIS AND METHOD OF MANUFACTURE**

2

3     FIELD OF THE INVENTION

4

5             The present invention relates to medical  
6     implants, particularly cardiac and vascular implants  
7     and prostheses. More specifically, the invention  
8     relates to a cardiac valve prosthesis comprising a  
9     frame and leaflets. Such valves may also be made  
10    without rigid frames and may also be used as valves  
11    in artificial hearts, whether the latter are intended  
12    for permanent implantation or for temporary support  
13    of a patient.

14

15    BACKGROUND OF THE INVENTION

16

17             In mammals the heart is the organ responsible  
18    for maintaining an adequate supply of blood, and  
19    hence of oxygen and nutrients, to all parts of the  
20    body. Reverse flow of blood through the heart is

1 prevented by four valves which serve as the inlet and  
2 outlet of each of the two ventricles, the pumping  
3 chambers of the heart.

4 Dysfunction of one or more of these valves can  
5 have serious medical consequences. Such dysfunction  
6 may result from congenital defects, or from disease  
7 induced damage. Forms of dysfunction include stenosis  
8 (reduction in the orifice of the open valve) and  
9 regurgitation (reverse flow through the closing or  
10 closed valve), either of which increases the work  
11 required by the heart to maintain the appropriate  
12 blood flows to the body.

13 In many cases the only effective solution is to  
14 replace the malfunctioning valve. A valve replacement  
15 operation is expensive and requires specialised  
16 facilities for open heart surgery. Replacement of  
17 failed artificial heart valves carries increased risk  
18 over the initial replacement, so there are practical  
19 limits on the number of times reoperation can be  
20 undertaken. Consequently, the design and materials of  
21 an artificial valve must provide for durability of  
22 the valve in the patient. The artificial valve must  
23 also operate without high pressure gradients or undue  
24 reverse flow during closing or when closed, because  
25 these are the very reasons for which a replacement of  
26 the natural valve is undertaken.

27 Mechanical valves, which use a ball or a disc or  
28 a pair of pivoting rigid leaflets as the opening  
29 member(s) can meet these combined requirements of  
30 haemodynamic performance and durability.  
31 Unfortunately, a patient who has had a mechanical

1 valve implanted must be treated with anticoagulants,  
2 otherwise blood will clot on the valve. Clotting on  
3 the valve can either restrict the movement of the  
4 valve opening member(s), impairing valve function, or  
5 can break free from the valve and obstruct blood  
6 vessels downstream from the valve, or both. A patient  
7 receiving a mechanical valve will be treated with  
8 anticoagulants for life.

9 Valves excised from pigs and treated with  
10 glutaraldehyde to crosslink and stabilise the tissue  
11 are also used for replacement of defective valves.  
12 These may be mounted on a more or less rigid frame,  
13 to facilitate implantation, or they may be unmounted  
14 and sewn by the surgeon directly to the vessel walls  
15 at operation. A further type of valve replacement is  
16 constructed from natural tissue, such as pericardium,  
17 treated with glutaraldehyde and mounted on a frame.  
18 Valves from pigs or made from other animal or human  
19 tissue are collectively known as tissue valves. A  
20 major advantage of tissue valves over mechanical  
21 valves is that they are much less likely to provoke  
22 the blood to clot, and so patients receiving tissue  
23 valves are not normally given anticoagulants other  
24 than during the immediate post operative period.  
25 Unfortunately, tissue valves deteriorate over time,  
26 often as a result of calcification of the crosslinked  
27 natural tissue. This deterioration presents a  
28 problem, particularly in young patients. Thus,  
29 although the recipient of a tissue valve is not  
30 required to take anticoagulants, the durability of  
31 tissue valves is less than that of mechanical valves.

1           In third world countries, where rheumatic fever  
2    is still common, the problems of valve replacement in  
3    young patients are considerable. Anticoagulants,  
4    required for mechanical valves, are impractical and  
5    accelerated calcification of tissue valves precludes  
6    their use.

7           In the Western world, life expectancy continues  
8    to increase, and this results in a corresponding rise  
9    both in patients requiring cardiac valve replacement,  
10   and in those patients needing replacement of  
11   deteriorating artificial valves implanted in the  
12   past. There is, therefore, a need for a replacement  
13   heart valve with good haemodynamics, extended  
14   durability and having sufficiently low risk of  
15   inducing clotting so that anticoagulants are not  
16   necessary.

17          The natural heart valves use thin flexible  
18    tissue leaflets as the closing members. The leaflets  
19    move readily out of the orifice as blood begins to  
20    flow through the valve so that flow through the open  
21    valve is unrestricted by the leaflets. Tissue valves  
22    function similarly, providing a relatively  
23    unrestricted orifice when the valve is open. For  
24    mechanical valves, on the other hand, the closing  
25    member rotates in the orifice, but is not removed  
26    from the orifice when the valve opens. This provides  
27    some restriction to flow, but, more importantly,  
28    disturbs the blood flow patterns. This disturbance to  
29    the flow is widely held to initiate, or at least to  
30    contribute significantly to, the observed tendency of  
31    mechanical valves to produce clotting.

1           A number of trileaflet polyurethane valve  
2     designs have been described.

3           A valve design, comprising a leaflet geometry  
4     which was elliptical in the radial direction and  
5     hyperbolic in the circumferential direction in the  
6     closed valve position, with leaflets dip-coated from  
7     non-biostable polyurethane solutions onto injection-  
8     moulded polyurethane frames has attained durabilities  
9     in excess of 800 million cycles during *in vitro*  
10    fatigue testing (Mackay TG, Wheatley DJ, Bernacca GM,  
11    Hindle CS, Fisher AC. New polyurethane heart valve  
12    prosthesis: design, manufacture and evaluation.  
13    *Biomaterials* 1996; 17:1857-1863; Mackay TG, Bernacca  
14    GM, Wheatley DJ, Fisher AC, Hindle CS. *In vitro*  
15    function and durability assessment of a polyurethane  
16    heart valve prosthesis. *Artificial Organs* 1996;  
17    20:1017-1025; Bernacca GM, Mackay TG, Wheatley DJ. *In*  
18    *vitro* function and durability of a polyurethane heart  
19    valve: material considerations. *J Heart Valve Dis*  
20    1996; 5:538-542; Bernacca GM, Mackay TG, Wilkinson R,  
21    Wheatley DJ. Polyurethane heart valves: fatigue  
22    failure, calcification and polyurethane structure. *J*  
23    *Biomed Mater Res* 1997; 34:371-379; Bernacca GM,  
24    Mackay TG, Gulbransen MJ, Donn AW, Wheatley DJ.  
25    Polyurethane heart valve durability: effects of  
26    leaflet thickness. *Int J Artif Organs* 1997; 20:327-  
27    331.). However, this valve design became  
28    unacceptably stenotic in small sizes. Thus, a  
29    redesign was effected, changing the hyperbolic angle  
30    from the free edge to the leaflet base, and replacing  
31    the injection-moulded frame with a rigid, high

1 modulus polymer frame. This redesign permitted the  
2 use of a thinner frame, thus increasing valve orifice  
3 area. This valve design, with a non-biostable  
4 polyurethane leaflet material, was implanted in a  
5 growing sheep model. Valve performance was good over  
6 the six month implant period, but the region close to  
7 the frame posts on the inflow side of the valve, at  
8 which full leaflet opening was not achieved, suffered  
9 a local accumulation of thrombus (Bernacca GM, Raco  
10 L, Mackay TG, Wheatley DJ. Durability and function of  
11 a polyurethane heart valve after six months *in vivo*.  
12 Presented at the XII World Congress of International  
13 Society for Artificial Organs and XXVI Congress of  
14 the European Society for Artificial Organs,  
15 Edinburgh, August 1999. Wheatley DJ, Raco L,  
16 Bernacca GM, Sim I, Belcher PR, Boyd JS.  
17 Polyurethane: material for the next generation of  
18 heart valve prostheses? Eur. J. Cardio-Thorac. Surg.  
19 2000; 17; 440-448). This valve design used non-  
20 biostable polyurethane, which had tolerable  
21 mechanical durability, but which showed signs of  
22 polymer degradation after six months *in vivo*.

23 International Patent Application WO 98/32400  
24 entitled "Heart Valve Prosthesis" discloses a similar  
25 design, i.e. closed leaflet geometry, comprising  
26 essentially a trileaflet valve with leaflets moulded  
27 in a geometry derived from a sphere towards the free  
28 edge and a cone towards the base of the leaflets. The  
29 spherical surface, defined by its radius, is intended  
30 to provide a tight seal when the leaflets are under  
31 back pressure, with ready opening provided by the

1 conical segment, defined by its half-angle, at the  
2 base of the leaflets. Were the spherical portion  
3 located at the leaflet base it is stated that this  
4 would provide an advantage in terms of the stress  
5 distribution when the valve is closed and under back  
6 pressure.

7 U.S. Patent No. 5,376,113 entitled "Closing  
8 Member Having Flexible Closing Elements, Especially a  
9 Heart Valve" issued December 27, 1994 to Jansen et  
10 al. discloses a method of producing flexible heart  
11 valve leaflets using leaflets attached to a base ring  
12 with posts extending from this upon which the  
13 leaflets are mounted. The leaflets are formed with  
14 the base ring in an expanded position, being  
15 effectively of planar sheets of polymer, which become  
16 flaccid on contraction of the ring. The resulting  
17 valve is able to maintain both a stable open and a  
18 stable closed position in the absence of any  
19 pulsatile pressure, though in the neutral unloaded  
20 position the valve leaflets contain bending stresses.  
21 As a consequence of manufacturing the valve from  
22 substantially planar sheets, the included angle  
23 between the leaflets at the free edge where they  
24 attach to the frame is  $60^\circ$  for a three leaflet valve.

25 U.S. Patent No. 5,500,016 entitled "Artificial  
26 Heart Valve" discloses a valve having a leaflet shape  
27 defined by the mathematical equation  $z^2 + y^2 = 2RL$   
28  $(x-g) - \alpha(x-g)^2$ , where  $g$  is the offset of the leaflet  
29 from the frame,  $RL$  is the radius of curvature of the  
30 leaflet at  $(g, 0, 0)$  and  $\alpha$  is the shape parameter and  
31 is  $>0$  and  $<1$ .



1           A valve design having a partially open  
2       configuration when the valve is not subject to a  
3       pressure gradient, but assuming a fully-open position  
4       during forward flow is disclosed in International  
5       Patent Application WO 97/41808 entitled "Method for  
6       Producing Heart Valves". The valve may be a  
7       polyurethane trileaflet valve and is contained within  
8       a cylindrical outer sleeve.

9           U.S. Patent Nos. 4,222,126 and 4,265,694  
10      disclose a trileaflet polyurethane valve with  
11      integral polyurethane elastomeric leaflets having  
12      their leading edges reinforced with an integral band  
13      of polymer and the leaflets reinforced radially with  
14      thicker lines of polyurethane.

15           The problem of chronic thrombus formation and  
16      tissue overgrowth arising from the suture ring of  
17      valves has been addressed by extension of the valve  
18      body on either side of the suture ring as disclosed  
19      in U.S. Patent No. 4,888,009 entitled "Prosthetic  
20      Heart Valve".

21           Current polyurethane valve designs have a number  
22      of potential drawbacks. Close coaptation of leaflets,  
23      while ensuring good valve closure, limits the wash-  
24      out of blood during haemodynamic function,  
25      particularly in the regions close to the stent posts  
26      at the commissures. This region of stagnation is  
27      likely to encourage local thrombogenesis, with  
28      further restriction of the valve orifice in the  
29      longer term as well as increasing the risk of  
30      material embolising into the circulation. Associated  
31      with the thrombosis may be material degradation (in

1 non-biostable polyurethanes) and calcification  
2 resulting in localised stiffening the leaflets,  
3 stress concentrations and leaflet failure. As  
4 previously discussed, animal implants of a trileaflet  
5 polyurethane valve design have indicated that  
6 thrombus does tend to collect in this region,  
7 restricting the valve orifice and damaging the  
8 structure of the valve.

9 Present valve designs are limited by the  
10 availability of suitable polyurethanes which possess  
11 good mechanical properties as well as sufficient  
12 durability to anticipate clinical functionality of up  
13 to twenty years or more. Many low modulus materials,  
14 which provide good hydrodynamic function, fail during  
15 fatigue testing at unacceptably low durations, due to  
16 their greater susceptibility to the effects of  
17 accumulated strain. Higher modulus polyurethanes may  
18 be better able to withstand repeated stress without  
19 accumulating significant damage, but are too stiff to  
20 provide good hydrodynamic function in conventional  
21 almost-closed geometry valve designs. Current design  
22 strategies have not been directed towards enabling  
23 the incorporation of potentially more durable, higher  
24 modulus leaflet materials, nor the creation of a  
25 valve design that is able to maintain good  
26 hydrodynamic function with low modulus polyurethanes  
27 manufactured as thick leaflets.

28 The nature of the valve leaflet attachment to  
29 the frame is such that, in many valve designs, there  
30 is a region of leaflet close to the frame, which is  
31 restrained by the frame. This region may extend some

1 distance into the leaflet before it interfaces with  
2 the free-moving part of the leaflet, or may be  
3 directly at the interface between frame and leaflet.  
4 There thus exists a stress concentration between the  
5 area of leaflet that is relatively mobile, undergoing  
6 transition between fully open and fully closed, and  
7 the relatively stationary commissural region. The  
8 magnitude of this flexural stress concentration is  
9 maximised when the design parameters predicate high  
10 bending strains in order for the leaflet to achieve  
11 its fully open position.

12 U.S. Patent Nos. 4,222,126 and 4,265,694  
13 disclose a valve which uses thickened leaflet areas  
14 to strengthen vulnerable area of the leaflets.  
15 However this approach is likely to increase the  
16 flexure stress and be disadvantageous in terms of  
17 leaflet hydrodynamic function.

18 The major difficulties which arise in designing  
19 synthetic leaflet heart valves can be explained as  
20 follows. The materials from which the natural  
21 trileaflet heart valves (aortic and pulmonary) are  
22 formed have deformation characteristics particularly  
23 suited to the function of such a valve. Specifically,  
24 they have a very low initial modulus, and so they are  
25 very flexible in bending, which occurs at low strain.  
26 This low modulus also allows the leaflet to deform  
27 when the valve is closed and loaded in such a way  
28 that the stresses generated at the attachment of the  
29 leaflets, the commissures, are reduced. The leaflet  
30 material then stiffens substantially, and this allows  
31 the valve to sustain the closed loads without

1 prolapse. Synthetic materials with these mechanical  
2 properties are not available.

3 Polyurethanes can be synthesised with good blood  
4 handling and good durability. They are available with  
5 a wide range of mechanical properties, although none  
6 has as low a modulus as the natural heart valve  
7 material. Although they show an increase in modulus  
8 at higher strains, this does not occur until strains  
9 much higher than those encountered in leaflet heart  
10 valves.

11 Polyurethanes have been the materials of choice  
12 for synthetic leaflet heart valves in the last decade  
13 or more. More recently, polyurethanes have become  
14 available which are resistant to degradation when  
15 implanted. They are clearly more suitable for making  
16 synthetic leaflet heart valves than non-stable  
17 polyurethanes, but their use suffers from the same  
18 limitations resulting from their mechanical  
19 properties. Therefore, design changes must be sought  
20 which enable synthetic trileaflet heart valves to  
21 function with the best available materials.

22 Key performance parameters which must be  
23 considered when designing a synthetic leaflet heart  
24 valve include pressure gradient, regurgitation, blood  
25 handling, and durability.

26 To minimise the gradient across the open valve,  
27 the leaflets must open wide to the maximum orifice  
28 possible, which is defined by the inside diameter of  
29 the stent. This means that there must be adequate  
30 material in the leaflets so they can be flexed into a  
31 tube of diameter equal to the stent internal

1 diameter. In addition, there has to be a low energy  
2 path for this bending because the pressure forces  
3 available to open the valve are small, and the lower  
4 the gradient, the smaller the pressure becomes. All  
5 the leaflets must open for the lowest cardiac output  
6 likely to be encountered by that valve in clinical  
7 service.

8 To minimise closing regurgitation (reverse flow  
9 lost through the closing valve ) the valve leaflets  
10 must be produced at or close to the closed position  
11 of the valve. To minimise closed valve regurgitation  
12 (reverse flow through the valve once it has closed),  
13 the apposition of the leaflets in the commissural  
14 region is found to be key, and from this perspective  
15 the commissures should be formed in the closed  
16 position.

17 Proper blood handling means minimising the  
18 activation both of the coagulation system and of  
19 platelets. The material of construction of the valve  
20 is clearly a very important factor, but flow through  
21 the valve must also avoid exposing blood either to  
22 regions of high shear (velocity gradient) or to  
23 regions of relative stasis. Avoiding regions of high  
24 shear is achieved if the valve opens fully, and  
25 relative stasis is avoided if the leaflet/frame  
26 attachment and the commissural region in particular  
27 opens wide. This is not achieved with typical  
28 synthetic materials when the commissures are molded  
29 almost closed, because the stiffness of synthetics is  
30 too high.

1           Durability depends to a large extent on the  
2 material of construction of the valve leaflets, but  
3 for any given material, lifetime will be maximised if  
4 regions of high stress are avoided. The loads on the  
5 closed valve are significantly greater than loads  
6 generated during valve opening. Therefore, the focus  
7 should be on the closed position. Stresses are  
8 highest in the region of the commissures where loads  
9 are transmitted to the stent, but they are reduced  
10 when the belly of the leaflet is as low as  
11 practicable in the closed valve. This means that  
12 there must be sufficient material in the leaflet to  
13 allow the desired low closing.

14

15   SUMMARY OF THE INVENTION

16

17           The present invention provides a cardiac valve  
18 prosthesis comprising a frame and two or more  
19 leaflets (preferably three) attached to the frame.  
20 The leaflets are attached to the frame between posts,  
21 with a free edge which can seal the leaflets together  
22 when the valve is closed under back pressure. The  
23 leaflets are created in a mathematically defined  
24 shape allowing good wash-out of the whole leaflet  
25 orifice, including the area close to the frame posts,  
26 thereby relieving the problem of thrombus deposition  
27 under clinical implant conditions.

28           The leaflet shape has a second design feature,  
29 by which the pressure required to open the valve and  
30 the pressure gradient across the valve in the open  
31 position is reduced by creating a valve which is

1 partially open in its stable unstressed position.  
2 Moulding the leaflets in a partially open position  
3 permits them to open easily to a wider angle  
4 resulting in an increased effective orifice area, for  
5 any given polyurethane/elastomeric material. This  
6 permits the use of materials from a wider range of  
7 mechanical properties to fabricate the leaflets,  
8 including those of a relatively stiff nature, and  
9 also permits lower modulus materials to be  
10 incorporated as thicker and hence more durable  
11 leaflets, while retaining acceptable leaflet  
12 hydrodynamic function.

13 A third design feature is the reduction of a  
14 stress concentration in the vicinity of the  
15 commissural region of the leaflets. In many valve  
16 designs, there exists a region of localised high  
17 bending where the opening part of the flexible  
18 leaflet merges into the stationary region of the  
19 leaflet adjacent to the valve frame. The current  
20 design reduces the bending, and hence the local  
21 stress concentration, in this region. This feature is  
22 designed to enhance the valve durability.

23 The wide opening of the leaflet coaptation close  
24 to the stent posts improves blood washout, reduces  
25 thrombogenesis and minimises embolic risks to the  
26 recipient, by allowing a clear channel for blood flow  
27 throughout the whole valve orifice.

28 The partially open design acts to reduce the  
29 fluid pressure required to open the valve. This in  
30 turn results in lower pressure gradients across the  
31 valve, allowing the use of durable, stiffer

1 polyurethanes to fabricate the valve which may be  
2 better equipped to deal with a cyclic stress  
3 application or thicker leaflets of lower modulus  
4 polyurethanes, hence achieving good durability with  
5 good hydrodynamic function. The position of the  
6 leaflet in its stable unstressed state acts to reduce  
7 the stress concentration resulting from leaflet  
8 bending, hence increasing valve durability.

9 In one aspect the invention is a cardiac valve  
10 prosthesis comprising a frame defining a blood flow  
11 axis and at least two leaflets attached to the frame.  
12 The at least two leaflets are configured to be  
13 movable from an open to a closed position. The  
14 leaflets have a blood inlet side and a blood outlet  
15 side and are in the closed position when fluid  
16 pressure is applied to the outlet side, and in the  
17 open position when fluid pressure is applied to the  
18 inlet side. The leaflets are in a neutral position  
19 intermediate the open and closed position in the  
20 absence of fluid pressure being applied to the  
21 leaflets. The at least two leaflets include a first  
22 leaflet. The first leaflet has a surface contour  
23 such that an intersection of the first leaflet with  
24 at least one plane perpendicular to the blood flow  
25 axis forms a first composite wave. The first  
26 composite wave is substantially defined by a first  
27 wave combined with at least a second wave  
28 superimposed over the first wave. The first wave has  
29 a first frequency and the second wave has a second  
30 frequency, different from the first frequency.  
31 Alternatively, the first composite wave may be



1 defined by a first wave combined with second and  
2 third waves superimposed over the first wave. The  
3 third wave has a third frequency which is different  
4 from the first frequency.

5 Both the first wave and the second wave may be  
6 symmetric or asymmetric about a plane parallel to and  
7 intersecting the blood flow axis and bisecting the  
8 first leaflet. The first composite wave may be  
9 symmetric or asymmetric about a plane parallel to and  
10 intersecting the blood flow axis and bisecting the  
11 first leaflet. The at least two leaflets may include  
12 second and third leaflets. An intersection of the  
13 second and third leaflets with a plane perpendicular  
14 to the blood flow axis forms second and third  
15 composite waves. The second and third composite  
16 waves are substantially the same as the first  
17 composite wave. The first and second waves may be  
18 defined by an equation which is trigonometric,  
19 elliptical, hyperbolic, parabolic, circular, a smooth  
20 analytic function or a table of values. The at least  
21 two leaflets may be configured such that they are  
22 substantially free of bending stresses when in the  
23 neutral position. The frame may be substantially  
24 cylindrical having first and second ends, one of the  
25 ends defining at least two scalloped edge portions  
26 separated by at least two posts, each post having a  
27 tip, and wherein each leaflet has a fixed edge joined  
28 to a respective scalloped edge portion of the frame  
29 and a free edge extending substantially between the  
30 tips of two posts. The first and second waves may be  
31 symmetric about a plane parallel to and intersecting

1 the blood flow axis and bisecting the first leaflet  
2 or at least one of the first and second waves may be  
3 symmetric about such plane. The first leaflet may  
4 have a surface contour such that when the first  
5 leaflet is in the neutral position an intersection of  
6 the first leaflet with a plane parallel to and  
7 intersecting the blood flow axis and bisecting the  
8 first leaflet forms a fourth wave.

9 In another aspect the invention is a method of  
10 making a cardiac valve prosthesis. The valve  
11 prosthesis includes a frame defining a blood flow  
12 axis substantially parallel to the flow of blood  
13 through the valve prosthesis and at least two  
14 flexible leaflets attached to the frame. The method  
15 includes providing a forming element having at least  
16 two leaflet forming surfaces. The forming element is  
17 engaged with the frame. A coating is applied over  
18 the frame and engaged forming element. The coating  
19 binds to the frame. The coating over the leaflet  
20 forming surfaces forms the at least two leaflets.  
21 The at least two leaflets are configured to be  
22 movable from an open to a closed position. The  
23 leaflets have a blood inlet side and a blood outlet  
24 side and are in the closed position when fluid  
25 pressure is applied to the outlet side, and in the  
26 open position when fluid pressure is applied to the  
27 inlet side. The leaflets are in a neutral position  
28 intermediate the open and closed position in the  
29 absence of fluid pressure being applied to the  
30 leaflets. The at least two leaflets include a first  
31 leaflet. The first leaflet has a surface contour

1 such that the intersection of the first leaflet with  
2 at least one plane perpendicular to the blood flow  
3 axis forms a first composite wave. The first  
4 composite wave is substantially defined by a first  
5 wave combined with a second superimposed wave. The  
6 first wave has a first frequency and the second wave  
7 has a second frequency different from the first  
8 frequency. After the coating is applied the forming  
9 element is disengaged from the frame. The first  
10 composite wave formed in the coating step may be  
11 defined by a first wave combined with second and  
12 third waves superimposed over the first wave. The  
13 third wave has a third frequency which is different  
14 from the first frequency.

15 The first and second waves formed in the coating  
16 step may be either symmetric or asymmetric about a  
17 plane parallel to and intersecting the blood flow  
18 axis and bisecting the first leaflet. The first  
19 composite wave formed in the coating step may be  
20 symmetric or asymmetric about a plane parallel to and  
21 intersecting the blood flow axis and bisecting the  
22 first leaflet. The at least two leaflets formed in  
23 the coating step may include second and third  
24 leaflets. An intersection of the second and third  
25 leaflets with a plane perpendicular to the blood flow  
26 axis forms second and third composite waves,  
27 respectively. The second and third composite waves  
28 are substantially the same as the first composite  
29 wave. The first and second waves formed in the  
30 coating step may be defined by an equation which is  
31 trigonometric, elliptical, hyperbolic, parabolic,

1 circular, a smooth analytic function or a table of  
2 values.

3 The first and second waves in the coating step  
4 may be symmetric about a plane parallel to and  
5 intersecting the blood flow axis and bisecting the  
6 first leaflet or at least one of the first and second  
7 waves may be asymmetric about such plane. The at  
8 least two leaflets in the coating step are configured  
9 such that they are substantially free of bending  
10 stresses when in the neutral position.

11 In a further aspect the invention is a cardiac  
12 valve prosthesis comprising a frame defining a blood  
13 flow axis and at least two leaflets attached to the  
14 frame including a first leaflet. The first leaflet  
15 has an internal surface facing the blood flow axis  
16 and an external surface facing away from the blood  
17 flow axis. The first leaflet is configured such that  
18 a mean thickness of a first half of the first leaflet  
19 is different than a mean thickness of a second half  
20 of the first leaflet. The first and second halves  
21 are defined by a plane parallel to and intersecting  
22 the blood flow axis and bisecting the first leaflet.  
23 The first leaflet may be further configured such that  
24 a thickness of the first leaflet between the internal  
25 and external surfaces along a cross section defined  
26 by the intersection of a plane perpendicular to the  
27 blood flow axis and the first leaflet changes  
28 gradually and substantially continuously from a first  
29 end of the cross section to a second end of the cross  
30 section.

1           In another aspect the invention is a method of  
2   making a cardiac valve prosthesis which includes a  
3   frame defining a blood flow axis substantially  
4   parallel to the flow of blood through the valve  
5   prosthesis and at least two flexible leaflets  
6   attached to the frame. The method includes providing  
7   a mould having a cavity sized to accommodate the  
8   frame, inserting the frame into the mould, inserting  
9   the mould into an injection moulding machine, and  
10   injecting molten polymer into the cavity of the mould  
11   to form the at least two leaflets. The injection of  
12   the molten polymer causes the at least two leaflets  
13   to bond to the frame. The cavity is shaped to form  
14   the at least two leaflets in a desired configuration.  
15   The at least two leaflets are configured to be  
16   movable from an open to a closed position. The  
17   leaflets have a blood inlet side and a blood outlet  
18   side and are in the closed position when fluid  
19   pressure is applied to the outlet side, and in the  
20   open position when fluid pressure is applied to the  
21   inlet side. The leaflets are in a neutral position  
22   intermediate the open and closed position in the  
23   absence of fluid pressure being applied to the  
24   leaflets. The at least two leaflets include a first  
25   leaflet having a surface contour such that when the  
26   first leaflet is in the neutral position an  
27   intersection of the first leaflet with at least one  
28   plane perpendicular to the blood flow axis forms a  
29   first composite wave. The first composite wave is  
30   substantially defined by a first wave combined with  
31   at least a second superimposed wave. The first wave

1 may have a first frequency, the second wave may have  
2 a second frequency, the first frequency being  
3 different from the second frequency.

4 In a still further aspect the invention is a  
5 method of designing a cardiac valve prosthesis which  
6 includes a frame and at least two flexible leaflets  
7 attached to the frame. The method includes defining  
8 a first desired shape of the leaflets in a first  
9 position, defining a second desired shape of the  
10 leaflets in a second position different from the  
11 first position, and conducting a draping analysis to  
12 identify values of adjustable parameters defining at  
13 least one of the first and second shapes. The  
14 draping analysis ensures that the leaflets are  
15 comprised of a sufficient amount and distribution of  
16 material for the leaflets to assume both the first  
17 and second desired shapes. Either of the first and  
18 second positions in the defining steps may be a  
19 closed position and the other of the first and second  
20 positions may be a partially open position.

21

## 22 DESCRIPTION OF DRAWINGS

23

24 FIG. 1 is a diagrammatic view comparing the  
25 shape of symmetric (solid line) and asymmetric  
26 (dashed line) leaflets.

27 FIG. 2 is a perspective view of the valve  
28 prosthesis in the neutral or partially open position.

29 FIG. 3 is a sectional view similar to the  
30 sectional view along line 3-3 of Fig. 2 except that  
31 Fig. 3 illustrates that view when the leaflets are in

1 the closed position and illustrates the function  
2 which is used to define the shape of the closed  
3 leaflet belly  $X_{Closed}(Z)$ .

4 FIG. 4A is a front view of the valve leaflet  
5 shown in Fig. 2. Fig. 4B is in the same view as Fig.  
6 4A and is a partial schematic view of the same closed  
7 valve leaflet shown in Fig. 3 and illustrates that  
8  $S(X, Y)_n$  and  $S(X, Y)_{n-1}$  are contours enclosing the  
9 leaflet between the function  $X_{Closed}(Z)$  and the scallop  
10 geometry.

11 FIG. 5 is a plot of an underlying function used  
12 in defining the valve leaflet in the moulded leaflet  
13 partially open position **P**.

14 FIG. 6 is a plot of a symmetrical superimposed  
15 function used in defining the shape of the valve  
16 leaflet in the moulded leaflet position **P**.

17 FIG. 7 is a plot of the composite function used  
18 in construction of the moulded leaflet position **P**  
19 resulting from combining an underlying function (Fig.  
20 5) and a symmetric superimposed function (Fig. 6).

21 FIG. 8 is a plot of an asymmetric superimposed  
22 function used in the construction of the moulded  
23 leaflet position **P**.

24 FIG. 9 is a plot of the composite function  
25 resulting from combining an underlying function  
26 (Fig. 5) and an asymmetric function (Fig. 8).

27 FIG. 10 is a sectional view of the valve  
28 leaflets in the neutral position along line 3-3 in  
29 Fig. 2 and illustrates the function which is used to  
30 define the shape of the moulded leaflet belly  
31  $X_{Open}(Z)$ .

1           FIG. 11A is a front view of the valve. Fig. 11B  
2           is a partial schematic view of the valve leaflets of  
3           Fig. 11A and illustrates that  $P(X, Y)_n$  and  $P(X, Y)_{n-1}$   
4           are contours enclosing the leaflet between the  
5           function  $X_{open}(Z)$  and the scallop geometry.

6           FIG. 12 is a perspective view of a valve of the  
7           present invention having symmetric leaflets.

8           FIG. 13 is a perspective view of a valve of the  
9           present invention having asymmetric leaflets.

10          FIG. 14 is a side view of a former used in the  
11          manufacture of the valve of the present invention.

12

#### 13          DESCRIPTION OF THE INVENTION

14

##### 15          a.     Design Considerations

16          Consideration of the factors discussed above  
17          results in the identification of certain design goals  
18          which are achieved by the prosthetic heart valve of  
19          the present invention. First, the prosthetic heart  
20          valve must have enough material in the leaflet for  
21          wide opening and low closing, but more than this  
22          amount increases the energy barrier to opening. To  
23          ensure that there is sufficient, but not an excess of  
24          material, a draping analysis discussed in more detail  
25          below is used. Second, to ensure sufficient material  
26          for wide opening and low closing, the valve can only  
27          be manufactured in a partially open position: (a) by  
28          deforming the stent posts outwards during  
29          manufacture; (b) by introducing multiple curves in  
30          the leaflet free edge (but see below); (c) by making  
31          the closed position asymmetric; and (d) combinations



1 of the above. Third, if there is enough material for  
2 low closing and wide opening, the energy barrier to  
3 opening may be high enough to prevent opening of all  
4 leaflets at low flow. The energy barrier can be  
5 minimised by: (a) introducing multiple curves in the  
6 leaflet; (b) making the leaflet asymmetric; and  
7 combinations of the above. Fourth, open commissures  
8 are needed for blood handling and closed commissures  
9 are needed for regurgitation, so the valve should  
10 have partially open commissures. In particular the  
11 included angle between adjacent leaflet free edges at  
12 the valve commissures (for example see angle  $\alpha$  of the  
13 symmetric leaflets shown in Fig. 1) should be in the  
14 range of 10-55°, preferably in the range 25-55° and  
15 more preferably in the range of 40-55°.

16 As discussed above, the use of multiple curves  
17 in the leaflet helps assure wide opening and more  
18 complete closure of the valve and to minimise the  
19 energy barrier to opening of the valve. However, the  
20 introduction of multiple curves of more than 1.5  
21 wavelengths to the leaflet can be a disadvantage.  
22 While there may be sufficient material in the leaflet  
23 to allow full opening, in order for this to happen,  
24 the bends in the leaflet must straighten out  
25 completely. The energy available to do this arises  
26 only from the pressure gradient across the open  
27 valve, which decreases as the leaflets becomes more  
28 open, i.e. as the valve orifice area increases. This  
29 energy is relatively small (the more successful the  
30 valve design the smaller it becomes), and does not  
31 provide enough energy to remove leaflet curves of

1 more than 1.5 wavelengths given the stiffness of the  
2 materials available for valve manufacture. The result  
3 is they do not straighten out and the valve does not  
4 open fully.

5 A draping analysis is used as a first  
6 approximation to full finite element analysis to  
7 determine if the starting shape of a membrane is such  
8 that it will take on a desired final shape when  
9 placed in its final position. From a durability  
10 standpoint the focus is on the closed position, and  
11 the desired shape of the leaflet in its closed  
12 position is defined. Draping analysis allows the  
13 leaflet to be reformed in a partially open position.

14 Draping analysis assumes that very low energy  
15 deformation is possible (in reality any form of  
16 deformation requires energy). In order for this to  
17 occur the bending stiffness of the leaflet/membrane  
18 must be small, each element of the membrane should be  
19 free to deform relative to its neighbour, and each  
20 element should be free to change shape, i.e. the  
21 shear modulus of the material is assumed to be very  
22 low. In applying the draping analysis, it is assumed  
23 that the leaflet can be moved readily from an  
24 original defined closed position to a new position in  
25 which it is manufactured. When the valve is actually  
26 cycled, it is assumed that the leaflet when closing  
27 will move from the manufactured position to the  
28 originally defined closed position. This allows the  
29 closed position to be optimized from a stress  
30 distribution aspect, and the manufactured position to

1 be optimized from the point of view of reducing the  
2 energy barrier to opening.

3 Both symmetric and asymmetric shapes of the  
4 leaflet can allow incorporation of sufficient  
5 material in the leaflet free edge to allow full  
6 opening. FIG. 1 is a diagrammatic view comparing the  
7 shape of symmetric (solid line) and asymmetric  
8 (dashed line) leaflets and also showing the  
9 commissure area 12 where the leaflets connect to the  
10 frame. An advantage of the asymmetric shape is that  
11 a region of higher radius of curvature 14 is produced  
12 than is achieved with a symmetric curve having a  
13 lower radius of curvature 16. This region can buckle  
14 more readily and thereby the energy barrier to  
15 opening is reduced.

16 An asymmetric leaflet also reduces the energy  
17 barrier through producing unstable buckling in the  
18 leaflet. During opening symmetric leaflets buckle  
19 symmetrically i.e. the leaflet buckles are generally  
20 mirrored about the centerline of the leaflet thus  
21 balancing the bending energies about this centerline.  
22 In the asymmetric valve the region of higher radius  
23 buckles readily, and because these bending energies  
24 are not balanced about the center line, this buckle  
25 proceeds to roll through the leaflet producing a  
26 sail-like motion producing a low energy path to open.

27 An additional feature of the asymmetric valve is  
28 that the open position is also slightly asymmetric,  
29 as a result of which it offers a somewhat helical  
30 flow path, and this can be matched to the natural  
31 helical sense of the aorta. Suggested benefits of

1     this helical flow path include reduction of shear  
2     stress non-uniformity at the wall, and consequent  
3     reduction of platelet activation.

4

5     b.     The Valve Prosthesis

6             The valve prosthesis will be described with  
7     reference to the accompanying drawings. Fig. 2 is a  
8     perspective view of one embodiment of the heart valve  
9     prosthesis of the present invention. The valve 10  
10    comprises a stent or frame 1 and attached leaflets  
11    2a, 2b, and 2c. The leaflets are joined to the frame  
12    at scallops 5a, 5b, and 5c. Between each scallop is  
13    post 8, the most down-stream part of which is known  
14    as a stent tip 6. Leaflets 2a, 2b, and 2c have free  
15    edges 3a, 3b, and 3c, respectively. The areas  
16    between the leaflets at the stent tips 6 form  
17    commissures 4.

18            The following describes a particular way of  
19    designing a valve of the present invention. Other  
20    different design methodology could be utilized to  
21    design a valve having the structural features of the  
22    valve disclosed herein. Five computational steps are  
23    involved in this particular method:

- 24            (1) Define the scallop geometry (the scallop, 5,  
25               is the intersection of the leaflet, 2, with  
26               the frame, 1);  
27            (2) Geometrically define a valve leaflet in the  
28               closed position C;  
29            (3) Map and compute the distribution of area  
30               across the leaflet in the closed position;

- 1       (4) Rebuild the leaflet in a partially open
- 2           position **P**; and
- 3       (5) Match the computed leaflet area distribution
- 4           in the partially open or moulded position **P**
- 5           to the defined leaflet in the closed position
- 6           **C**. This ensures that when an increasing
- 7           closing pressure is applied to the leaflets,
- 8           they eventually assume a shape which is
- 9           equivalent to that defined in closed position
- 10          **C**.

11           This approach allows the closed shape of the  
 12    leaflets in position **C** to be optimised for durability  
 13    while the leaflets shaped in the moulded partially  
 14    open shape **P** can be optimised for haemodynamics. This  
 15    allows the use of stiffer leaflet materials for  
 16    valves which have good haemodynamics. An XYZ co-  
 17    ordinate system is defined as shown in Fig. 2, with  
 18    the Z axis in the flow direction of blood flowing  
 19    through the valve.

20           The leaflets are mounted on the frame, the shape  
 21    of which results from the intersection of the  
 22    aforementioned leaflet shape and a 3-dimensional  
 23    geometry that can be cylindrical, conical or  
 24    spherical in nature. A scallop shape is defined  
 25    through intersecting the surface enclosed by the  
 26    following equations with a cylinder of radius **R**  
 27    (where **R** is the internal radius of the valve):

$$X_{ell} = E_{s0} - E_{sj} \cdot \sqrt{1 - \left( \frac{Z}{E_{sN}} \right)^2}$$

$$H_{sJ} = E_{sO} - E_{sJ} \sqrt{1 - \left( \frac{Z}{E_{sN}} \right)^2} - H_{sO}$$

$$H_{sN}(Z) = H_{sJ} \cdot \tan(60) \cdot f(Z)$$

1 where  $f(Z)$  is a function changing with  $Z$ .

$$X_{hyp} = H_{sO} + H_{sJ} \sqrt{1 - \left( \frac{Y}{H_{sN}} \right)^2}$$

2 The shape of the scallop can be varied using the  
 3 constants  $E_{sO}$ ,  $E_{sJ}$ ,  $H_{sO}$ ,  $f(Z)$ . The definition of  
 4 parameters used in these and the other equations  
 5 herein are contained in Table 4.

6 The shape of the leaflet under back pressure  
 7 (i.e. in the closed position **C**) can be approximated  
 8 mathematically using elliptical or hyperbolic co-  
 9 ordinates, or a combination of the above in an XYZ  
 10 co-ordinate system where XY is the plane of the valve  
 11 perpendicular to the blood flow and Z is the  
 12 direction parallel to the blood flow. The parameters  
 13 are chosen to define approximately the shape of the  
 14 leaflet under back pressure so as to allow convenient  
 15 leaflet re-opening and minimise the effect of the  
 16 stress component which acts in the direction parallel  
 17 to the blood flow, whilst also producing an effective  
 18 seal under back pressure.

19 The closed leaflet geometry in closed position **C**  
 20 is chosen to minimise stress concentrations in the  
 21 leaflet particularly prone to occur at the valve  
 22 commissures. The specifications for this shape  
 23 include:

- 1 (1) inclusion of sufficient material to allow a
- 2 large open-leaflet orifice;
- 3 (2) arrangement of this material to minimise
- 4 redundancy (excess material in the free edge,
- 5 3) and twisting in the centre of the free
- 6 edge, 3; and
- 7 (3) arrangement of this material to ensure the
- 8 free edge, 3, is under low stress i.e.
- 9 compelling the frame and leaflet belly to
- 10 sustain the back-pressure.

11 Fig. 3 is a partial sectional view (using the  
 12 section 3-3 shown in Fig. 2) showing only the  
 13 intended position of the leaflet in the closed  
 14 position. The shape of this intended position is  
 15 represented by the function  $X_{Closed}(Z)$ . This function  
 16 can be used to arrange the shape of the leaflet in  
 17 the closed position **C** to meet the aforementioned  
 18 specification. The curve is defined using the  
 19 following equation and manipulated using the  
 20 constants  $E_{cJ}$ ,  $E_{cO}$ ,  $Z_{cO}$  and the functions  $E_{cN}(Z)$  and  
 21  $X_T(Z)$ .

$$X_{Closed}(Z) = - \left[ E_{cJ} \left( 1 - \left( \frac{Z - Z_{cO}}{E_{cN}(Z)} \right)^2 \right) \right]^{0.5} + E_{cO} - X_T(Z)$$

22 where  $E_{cN}$  is a function changing linearly with  $Z$  and  
 23  $X_T(Z)$  is a function changing nonlinearly with  $Z$ .

24 Thus the scallop shape and the function  $X_{Closed}(Z)$   
 25 are used to form the prominent boundaries for the  
 26 closed leaflet in the closed position **C**. The

1 remaining part of the leaflet is formed using  
2 contours  $S(X, Y)_n$  sweeping from the scallop to the  
3 closed leaflet belly function  $X_{closed}(Z)$ , where  $n$  is an  
4 infinite number of contours, two of which are shown  
5 in Fig. 4B.

6 The length of the leaflet (or contours  $S(X, Y)_n$ )  
7 in the circumferential direction (XY) is calculated  
8 and repeated in the radial direction (Z) yielding a  
9 function  $L(Z)$  which is used later in the definition  
10 of the geometry in the partially open position  $P$ . The  
11 area contained between respective contours is also  
12 computed yielding a function  $K(Z)$  which is also used  
13 in the definition of the geometry in position  $P$ . The  
14 area contained between contours is approximated using  
15 the process of triangulation as shown in Fig. 4B.  
16 This entire process can be shortened by reducing the  
17 number of contours used to represent the surface  
18 ( $100 < n < 200$ ).

19 The aforementioned processes essentially define  
20 the leaflet shape and can be manipulated to optimise  
21 for durability. In order to optimise for  
22 haemodynamics, the same leaflet is moulded in a  
23 position  $P$  which is intermediate in terms of valve  
24 opening. This entails moulding large radius curves  
25 into the leaflet which then serve to reduce the  
26 energy required to buckle the leaflet from the closed  
27 to the open position. The large radius curves can be  
28 arranged in many different ways. Some of these are  
29 outlined herein.

30 The leaflet may be moulded on a dipping former  
31 as shown in Fig. 14. Preferably the former is tapered



1 with an included angle  $\theta$  so that the end 29 has a  
2 diameter which is greater than the end 22. (This  
3 ensures apposition of the frame and former during  
4 manufacture.). In this case, the scallop shape,  
5 defined earlier, is redefined to lie on a tapered  
6 geometry (as opposed to the cylindrical geometry used  
7 in the definition of the closed leaflet shape). This  
8 is achieved by moving each point on the scallop  
9 radially, and in the same movement, rotation of each  
10 point about an X-Y plane coincident with the bottom  
11 of the scallop, until each point lies on the tapered  
12 geometry.

13 The geometry of the leaflet shape can be defined  
14 as a trigonometric arrangement (or other mathematical  
15 function) preferably sinusoidal in nature in the XY  
16 plane, comprising one or more waves, and having  
17 anchoring points on the frame. Thus the valve  
18 leaflets are defined by combining at least two  
19 mathematical functions to produce composite waves,  
20 and by using these waves to enclose the leaflet  
21 surface with the aforementioned scallop.

22 One such possible manifestation is a composite  
23 curve consisting of an underlying low frequency  
24 sinusoidal wave upon which a second higher frequency  
25 sinusoidal wave is superimposed. A third wave having  
26 a frequency different from the first and second waves  
27 could also be superimposed over the resulting  
28 composite wave. This ensures a wider angle between  
29 adjacent leaflets in the region of the commissures  
30 when the valve is fully open thus ensuring good wash-  
31 out of this region.

1           The composite curve, and the resulting leaflet,  
 2   can be either symmetric or asymmetric about a plane  
 3   parallel to the blood flow direction and bisecting a  
 4   line drawn between two stent tips such as, for  
 5   leaflet 2a, the section along line 3-3 of Fig. 2.  
 6   The asymmetry can be effected either by combining a  
 7   symmetric underlying curve with an asymmetric  
 8   superimposed curve or *vice versa*.

9           The following describes the use of a symmetric  
 10   underlying function with an asymmetric superimposed  
 11   function, but the use of an asymmetric underlying  
 12   function will be obvious to one skilled in the art.  
 13   The underlying function is defined in the XY plane  
 14   and connects the leaflet attachment points to the  
 15   scallop at a given height from the base of the valve.  
 16   This underlying function shown in Fig. 5, can be  
 17   trigonometric, elliptical, hyperbolic, parabolic,  
 18   circular, or other smooth analytic function or could  
 19   be a table of values.

20          Using sine functions, one possible underlying  
 21   wave is shown in Fig. 5 and is defined using the  
 22   following equation.

$$X_u = X_{(u,0)} + A_u \cdot \sin \left[ \left( \frac{0.5\pi}{Y_{(u,0)}} \right) (Y - Y_{(u,0)}) \right]$$

23          The superimposed wave is defined in the XY  
 24   plane, and connects the attachment points of the  
 25   leaflet to the scallop at a given height above the  
 26   base of the valve. The superimposed wave is of higher  
 27   frequency than the underlying wave, and can be

1 trigonometric, elliptic, hyperbolic, parabolic,  
 2 circular, or other smooth analytic function, or a  
 3 table of values.

4 Using sine functions, one possible symmetric  
 5 leaflet design is formed when the underlying wave is  
 6 combined with a superimposed wave formed using the  
 7 following equation.

$$X_s = -A_s \cdot B_s(Y) \sin \left[ \left( \frac{1.5\pi}{Y_{(n,0)}} \right) (Y - Y_{(n,0)}) \right]$$

8  $A_s$  can be varied across the leaflet to produce  
 9 varying wave amplitude across the leaflet, for  
 10 example lower amplitude at the commissures than in  
 11 the leaflet centre.  $B_s$  can be varied to adjust the  
 12 length of the wave. The superimposed wave is shown  
 13 in Fig. 6. The composite wave formed by combining  
 14 the underlying wave (Fig. 5) with the superimposed  
 15 wave (Fig. 6) is shown in Fig. 7.

16 Using sine functions, one possible asymmetric  
 17 leaflet design is formed when the underlying wave  
 18 (Fig. 5) is combined with a superimposed wave formed  
 19 using the following equation.

$$X_s = -A_s \cdot B_s(Y) \sin \left[ \left( \frac{\pi}{Y_{(n,0)}} \right) (Y - Y_{(n,0)}) \right]_0^{Y_{(n,0)}}$$

$$X_s = 0.5 \cdot A_s \cdot B_s(Y) \sin \left[ \left( \frac{2.0\pi}{Y_{(n,0)}} \right) Y \right]_{(-Y_{(n,0)})}^0$$

1            $A_s$  can be varied across the leaflet to produce  
 2   varying wave amplitude across the leaflet, for  
 3   example lower amplitude at the commissures than in  
 4   the leaflet centre.  $B_s(Y)$  can be varied to adjust the  
 5   length of the wave. The superimposed wave is shown  
 6   in Fig. 8. The resulting asymmetric composite wave  
 7   is shown in Fig. 9. The composite wave  $W(X_c, Y_c)_n$  is  
 8   created by offsetting the superimposed wave normal to  
 9   the surface of the underlying wave (Figs. 7, 9).

10           While the general shape of the leaflet in  
 11   position  $P$  has been determined using the composite  
 12   wave, at this stage it is not specified in any  
 13   particular position. In order to specify the position  
 14   of  $P$ , the shape of the partially open leaflet  
 15   position can be defined as  $X_{open}(Z)$ . This is shown as  
 16   reference numeral 7 in Fig. 10.

17           One possible function determining this shape is  
 18   given as follows:

$$X_{open}(Z) = - \left[ E_{oJ} \left( 1 - \left( \frac{Z - Z_{oQ}}{E_{oN}} \right)^2 \right) \right]^{0.5} + E_{oO}$$

19           In order to manipulate the composite wave to  
 20   produce the belly shape  $X_{open}(Z)$  the respective  
 21   amplitudes of the individual sine waves can be varied  
 22   from the free edge to the leaflet base. For example,  
 23   the degree of 'openness' of the leaflet in position  $P$   
 24   can be varied throughout the leaflet.

25           The composite wave is thus defined to produce  
 26   the moulded "buckle" in the leaflet, and  $X_{open}(Z)$  is  
 27   used to define the geometry of the leaflet at

1 position  $P$ . At this stage it may bear no  
2 relation to the closed leaflet shape in position  $C$ .  
3 In order to match the area distribution of both  
4 leaflet positions, (thus producing essentially the  
5 same leaflet in different positions) the composite  
6 wave length is iterated to match the length of the  
7 relevant leaflet contour in position  $C$ . Thus the  
8 amplitude and frequency of the individual waves can  
9 be varied in such a manner as to balance between: (a)  
10 producing a resultant wave the length of which is  
11 equal to the relevant value in the length function  
12  $L(Z)$  thus approximating the required closed shape  
13 when back pressure is applied, and (b) allowing  
14 efficient orifice washout and ready leaflet opening.  
15 Also the area contained between the contours in the  
16 open leaflet is measured using the same process of  
17 triangulation as in the closed position  $C$ , and is  
18 iterated until it matches with the area contained  
19 between relevant contours in position  $C$  (denoted  
20  $K(Z)$ ) (through tilting the contours in  $P$  relative to  
21 each other). Thus the composite waves  $(P(X, Y)_n)$   
22 pertaining to the contour  $n$  and length  $L(Z)$  can be  
23 tilted at an angle to the  $XY$  plane about attachment  
24 points  $X_{(n,0)}$ ,  $Y_{(n,0)}$  and  $X_{(n,0)}$ ,  $-Y_{(n,0)}$  until the correct  
25 area is contained between  $P(X, Y)_n$  and  $P(X, Y)_{n-1}$  (See  
26 Figs. 10 & 11).

27 This process identifies the values of  $B_s$ ,  $A_u$  and  
28 the contour tilt angle to be used in constructing the  
29 mould for the valve leaflet. As long as the constants  
30 such as  $B_s$  and  $A_u$ , and the tilt angle of the contours  
31 relative to the  $XY$  plane, are known, the surface of

1 the leaflet in its moulded position can be  
2 visualised, enclosed and machined in a conventional  
3 manner. As a result of this fitting process the  
4 composite wave retains the same basic form but  
5 changes in detail from the top of the leaflet to the  
6 bottom of the leaflet. A composite wave can be  
7 defined in the leaflet surface as the intersection of  
8 the leaflet surface with a plane normal to the Z  
9 axis. This composite wave will have the same general  
10 form as the composite wave used in the leaflet design  
11 but will differ from it in detail as a result of the  
12 tilting process described above.

13 In summary therefore one possible method of  
14 designing the leaflet according to the present  
15 invention is in the following way:

- 16 (1) Define a scallop shape;
- 17 (2) Define a shape approximating the shape of the  
18 closed leaflet using elliptical, hyperbolic,  
19 parabolic or circular functions, smooth  
20 analytical functions or table of values;
- 21 (3) Compute the functions  $L(Z)$  and  $K(Z)$ , which  
22 define the length of the leaflet in the XY  
23 plane along the Z axis and the area  
24 distribution of the leaflet along the Z axis;
- 25 (4) Use one or more associated sine waves to  
26 generate a geometry which is partially-open,  
27 which pertains to a leaflet position which is  
28 between the two extreme conditions of normal  
29 valve function, i.e. leaflet open and leaflet  
30 closed;

1       (5) Vary the frequency and amplitude of the  
2           sinewaves to fit to the length function  $L(Z)$   
3           and the angle at which the contour is tilted  
4           to the XY plane to fit to the area function  
5            $K(Z)$ ; and

6       (6) The respective amplitudes of the individual  
7           sine waves can be varied from the free edge  
8           to leaflet base, for example the degree of  
9           'openness' of the leaflet can be varied  
10          throughout the leaflet.

11       Herein are some examples of how this invention  
12       can be put into practice. Using the scallop constants  
13       in Table 1, the constants required to produce an  
14       example of a symmetric leaflet valve and an example  
15       of an asymmetric leaflet valve are given in Table 2  
16       and Table 3 respectively. These constants are used in  
17       conjunction with the aforementioned equations to  
18       define the leaflet geometry.

19       With one leaflet described using the  
20       aforementioned equations, the remaining two leaflets  
21       are generated by rotating the geometry about the Z  
22       axis through  $120^\circ$  and then through  $240^\circ$ . These  
23       leaflet shapes are inserted as the leaflet forming  
24       surfaces of the dipping mould (otherwise known as a  
25       dipping former), which then forms a 3-dimensional  
26       dipping mould. The composite wave described in the  
27       aforementioned equations, therefore substantially  
28       defines the former surface which produces the inner  
29       leaflet surface.

30       As seen in Fig. 14 the dipping mould 20 is  
31       slightly tapered so that the end 29 has a diameter

1 which is greater than the end 22, and has a first end  
2 22 having an outside diameter slightly smaller than  
3 the inside diameter of the frame. The former  
4 includes at least two and preferably three leaflet  
5 forming surfaces 24 which are defined by scalloped  
6 edges 26 and flats 28. Sharp edges in the  
7 manufacturing former and on the frame are radiused to  
8 help reduce stress concentrations in the finished  
9 valve. During the dip moulding process the frame is  
10 inserted over end 22 of the former so that the  
11 scallops 5 and stent posts 8 of the frame align with  
12 the scalloped edges 26 and flats 28 of the former.  
13 The leaflet forming surfaces 24 are configured to  
14 form leaflets during the moulding process which have  
15 the geometry described herein. This mould can be  
16 manufactured by various methods, such as, machining,  
17 electrical discharge machining, injection moulding.  
18 In order that blood flow is not disturbed, a high  
19 surface finish on the dipping mould is essential.

20 For the frame there are preferably three posts  
21 with leaflets hung on the frame between the posts. A  
22 crown-like frame or stent, 1, is manufactured with a  
23 scallop geometry, which matches the dipping mould  
24 scallop. The frame scallop is offset radially by  
25 0.1mm to allow for the entire frame to be coated with  
26 a thin layer of leaflet material to aid adhesion of  
27 the leaflets. Leaflets may be added to the frame by a  
28 dip-moulding process, using a dipping former machined  
29 or moulded to create the multiple sinewave form.

30 The material of preference should be a semi-  
31 rigid fatigue- and creep-resistant frame material



1 such as PEEK, high modulus polyurethane, titanium,  
2 reinforced polyurethane, or polyacetal (Delrin)  
3 produced by machining or injection-moulding etc.  
4 Alternatively, a relatively low modulus polymer may  
5 be used, which may be fibre-reinforced, to more  
6 closely mimic the aortic wall. The frame can be  
7 machined or injection moulded, and is manufactured  
8 preferably from polyetheretherketone (PEEK) or  
9 polyacetal (Delrin).

10 The first stage of valve manufacture entails  
11 dipping the frame in a polyurethane solution  
12 (preferably Elast-Eon<sup>TM</sup> manufactured by Elastomedic,  
13 Sydney Australia) in order to apply a coating of  
14 approximately 0.1mm thick. Having dried the frame  
15 with applied coating in an oven overnight, it is  
16 placed on the dipping former and aligned with the  
17 former scallops. The combination of frame and three  
18 dimensional dipping mould is then dipped into  
19 polyurethane solution, which forms a coating of  
20 solution on frame and mould. This coating flows  
21 slowly over the entire mould surface ensuring a  
22 smooth coating. The new coating on the frame and  
23 dipping mould solvates the initial frame coating thus  
24 ensuring a good bond between leaflet and frame. The  
25 dipping mould with polyurethane covering is dried in  
26 an oven until all the solvent has been removed. One  
27 or more dips may be used to achieve a leaflet with a  
28 mean thickness between 40µm and 500µm. The shape of  
29 the former, and the viscosity and solvent interactive  
30 properties of the polyurethane solution, control the  
31 leaflet thickness and the distribution of thickness

1 over the leaflet. A dipping process does not allow  
2 precise control of leaflet thickness and its  
3 variation across a leaflet. In particular surfaces  
4 that are convex on the dipping former result in  
5 reduced leaflet thickness when compared with surfaces  
6 that are concave. Additionally the region of the  
7 leaflet adjacent to the frame essentially provides a  
8 very small concave radius which traps further polymer  
9 solution and this results in thickening of these  
10 regions.

11 The shape of the former is substantially defined  
12 by the composite wave. Radiusing and polishing of  
13 the former can both contribute to some variation of  
14 the shape. The shape of the inner surface of the  
15 leaflets will closely replicate the shape of the  
16 former. The shape of the outer surface of the  
17 leaflets will be similar to the shape of the inner  
18 surface but variations will result from the  
19 processing properties of the polymer solution and  
20 details of the dipping process used to produce the  
21 valve. The leaflet may be formed from polyurethanes  
22 having a Young's modulus less than 100MPa, preferably  
23 in the range 5 to 50 MPa.

24 The valve is next removed from the dipping  
25 mould. The stent posts, which had been deflected by  
26 the taper on the former, now recover their original  
27 position. The shape of the leaflets changes slightly  
28 as a result of the movement of the stent posts.

29 At this stage the dipping mould and frame is  
30 covered with an excess of polyurethane due to the  
31 drain-off of the polymer onto the region of the mould

1 known as the drain-off area 30. Leaflet free edges  
2 may be trimmed of excess material using a sharp blade  
3 rotated around the opened leaflets or using laser-  
4 cutting technology.

5 An alternate valve manufacturing method is  
6 injection moulding. A mould is constructed with a  
7 cavity which allows the valve frame to be inserted in  
8 the mould. The cavity is also designed with the  
9 leaflet geometry, as defined above, as the inner  
10 leaflet surface. A desired thickness distribution is  
11 defined for the leaflet and the outer leaflet surface  
12 of the mould is constructed by adding the leaflet  
13 thickness normally to the inner leaflet surface. The  
14 leaflet may be of uniform thickness throughout, in  
15 the range 40 to 500 microns, preferably 50 to 200  
16 microns, more preferably 80 to 150 microns. The  
17 leaflet may be thickened towards its attachment to  
18 the frame. Alternatively the thickness of the  
19 leaflet, along a cross-section defined by the  
20 intersection of a plane perpendicular to the blood  
21 flow axis and the leaflet, can change gradually and  
22 substantially continuously from a first end of the  
23 cross-section (i.e. first edge of the leaflet) to a  
24 second end of the cross-section (i.e. second edge of  
25 the leaflet) in such a way that the mean thickness of  
26 the first half of the leaflet is different from the  
27 mean thickness of the second half of the leaflet.  
28 This mould is inserted in a conventional injection  
29 moulding machine, the frame is inserted in the mould  
30 and the machine injects molten polymer into the  
31 cavity to form the leaflets and bond them to the

1 frame. The polymer solidifies on cooling and the  
2 mould is opened to allow the complete valve to be  
3 removed.

4 The leaflets may also be formed using a  
5 reaction-moulding process (RIM) whereby the polymer  
6 is synthesised during the leaflet forming. A mould is  
7 constructed as described above. This mould is  
8 inserted in a reaction-injection moulding machine,  
9 the frame is inserted in the mould and the machine  
10 injects a reactive mixture into the cavity. The  
11 polymer is produced by the reaction in the cavity to  
12 form the leaflets and bond them to the frame. When  
13 the reaction is complete, the mould is opened to  
14 allow the complete valve to be removed.

15 Yet a further option is to compression mould a  
16 valve initially dipped. This approach allows the  
17 leaflet thickness or thickness distribution to be  
18 adjusted from that initially produced. By varying  
19 the thickness of the leaflets the dynamics of the  
20 valve opening and closing can be modified. For  
21 example, the thickness of the leaflet along a cross-  
22 section defined by the intersection of a plane  
23 perpendicular to the blood flow axis and the leaflet  
24 can be varied so that the thickness changes gradually  
25 and substantially continuously from a first end of  
26 the cross-section (i.e. first edge of the leaflet) to  
27 a second end of the cross-section (i.e. second edge  
28 of the leaflet) in such a way that the mean thickness  
29 of the first half of the leaflet is different from  
30 the mean thickness of the second half of the leaflet.  
31 This will result in the thinner half of the leaflet

1 opening first and creating a sail-like opening motion  
2 along the free edge of the leaflet.

3 Leaflet shape resulting from conventional  
4 injection moulding, reaction injection moulding or  
5 compression moulding, is substantially defined by the  
6 composite wave described above. It will differ in  
7 detail for many of the same reasons identified for  
8 dip moulding.

9 The valves of the present invention are  
10 manufactured in the neutral position or close to it  
11 and are therefore substantially free of bending  
12 stresses in this position. As a result when the  
13 leaflet is moved to its closed position the total  
14 bending energy at the leaflet center free edge and at  
15 the commissures is reduced compared to a valve made  
16 according to U.S. Patent No. 5,376,113.

17 The valves of the present invention may be used  
18 in any required position within the heart to control  
19 blood flow in one direction, or to control flow  
20 within any type of cardiac assist device.

21 The following examples use the same scallop  
22 geometry described using the constants set forth in  
23 Table 1: While the examples described herein relate  
24 to one valve size, the same method can be used to  
25 produce valves from a wide range of sizes. This can  
26 be carried out by modifying the constants used in the  
27 equations, by rescaling the bounding curves such as  
28  $X_{closed}(Z)$  and computing and iterating in the normal  
29 fashion or by rescaling the leaflet.

30

31

	values (mm)
$R$	11.0
$E_{SO}$	21.7
$E_{SJ}$	21.5
$E_{SN}$	13.8
$H_{SO}$	0.18
$f(Z)$	$(0.05 \cdot Z) + 1.0$

Table 1

1 Example 1.

2       The parameters described in the preceding  
3 sections are assigned the values set forth in Table 2  
4 and are used to manufacture a symmetric valve. The  
5 included angle between adjacent leaflet free edges at  
6 the valve commissure for this valve is approximately  
7 50°.

Parameter	Value (mm)
<i>Closed position</i>	
$Z_{CO}$	0
$Z_{CO}$	0.0
$E_{CN}(Z)$	$E_{CN}=3.0 \cdot Z+50.3$
$E_{CO}$	22.0
$E_{CJ}$	20.0
$X_T(Z)$	0.0
<i>Partially-open position</i>	
$\theta$	12.7°
$E_{OJ}$	50.0

$Z_{oo}$	4.0
$E_{oo}$	51.8
$E_{oN}$	27.7
$A_u$	Result from iteration procedure finds that $A_u$ varies from $1e-5$ at the leaflet base to 5.1 at 4mm from the leaflet base to 3.8 at the free edge.
$A_s$	Result from iteration procedure finds that $A_s$ varies from $1e-3$ at the leaflet base to 1.6 at 3mm from the leaflet base to 0.6 at the free edge.
$B_s(Y)$	1.0

Table 2

1            Fig. 12 shows the symmetric valve which is  
2    manufactured, using the values outlined in Table 1  
3    and Table 2.

4

5    Example 2

6            The parameters described in the preceding  
7    sections are assigned the values set forth in Table 3  
8    and are used to manufacture an asymmetric valve. The  
9    included angle between adjacent leaflet free edges at  
10   the valve commissure for this valve is approximately  
11    $48^\circ$ .

<b>Parameter</b>	<b>Value (mm)</b>
<i>Closed position</i>	
$Z_{co}$	0.0
$E_{cN}(Z)$	$E_{cN}=3.0.Z+48.9$
$E_{co}$	18.4
$E_{cJ}$	20.0
$X_{T(Z)}$	$X_{T(n-1)}=0.97.(X_{T(n)})$ where $X_{T(free\ edge)}=2.1$
<i>Partially-open position</i>	
$\theta$	$7.1^\circ$
$E_{oJ}$	50.0
$Z_{oo}$	5.0
$E_{oo}$	51.5
$E_{oN}$	29.0
$A_u$	Result from iteration procedure finds that $A_u$ varies from $1e-5$ at the leaflet base to 3.1 at 3mm from the leaflet base to 2.2 at 9mm from the leaflet base to 3.8 at the free edge.
$A_s$	Result from iteration procedure finds that $A_s$ varies from $1e-3$ at the leaflet base to 1.1 at 6mm from the leaflet base to 0.4 at the free edge.
$B_s(Y)$	$B_s(Y)=(Y-c)/m$ where $B_s=1$ at leaflet base and $m=5.04$ and $c=-15.1$ at leaflet free edge.

**Table 3**

1            Fig. 13 shows the valve which is manufactured  
2    using the values outlined in Table 1 and Table 3.  
3



<b>Definition of parameters</b>	
<b>R</b>	Internal radius of valve
<b>Scallop (Fig. 2)</b>	
$X_{ell}$ , $H_{SJ}$ , $H_{SN}$ , $X_{hyp}$ are used to define a surface which, when intersected with a cylinder, scribe a function which forms the scallop for one leaflet. This method for creating a scallop is described in Mackay et al. Biomaterials 17 1996. although an added variable $f(Z)$ is used for added versatility.	
$X_{ell}$	Scribes an ellipse in the radial direction.
$X_{hyp}$	Scribes a hyperbola in the circumferential direction.
$E_{SO}$	Ellipse X-axis offset
$E_{SJ}$	Major axis of the ellipse
$E_{SN}$	Minor axis of the ellipse
$H_{SJ}$	Major axis of the hyperbola
$H_{SN}$	Minor axis of the hyperbola
$H_{SO}$	Hyperbola x-axis offset
$f(Z)$	Creates a varying relationship between $H_{SN}$ and $H_{SJ}$
<b>Closed Leaflet geometry C (Figs. 3 &amp; 4)</b>	
$X_{closed}(Z)$ is defined as an ellipse (with a minor axis $E_{CN}(Z)$ which changes with Z) in the $XZ$ axis in the plane defined in Fig. 2 by cutting plane 3-3. It is defined using the following constants and functions.	

$Z_{co}$	Closed ellipse Z-axis offset
$E_{CN}(Z)$	Closed ellipse minor axis which changes with Z
$E_{co}$	Closed ellipse X-axis offset
$E_{cJ}$	Closed ellipse major axis
$X_T(z)$	Offset function which serves to increase the amount of material in the belly
<b>Moulded position P</b>	
<p><b>P</b> is enclosed by a number (n) of contours <math>P(X,Y)_n</math> which run from one side of the scallop to the other. The underlying function <math>X_u</math> is used in defining both symmetric and asymmetric leaflets. <math>X_u</math> is simply an ellipse (or other such function) running in a plane from one side of the scallop to the other. The points on the scallop are designated <math>X_{(n,0)}</math>, <math>Y_{(n,0)}</math> where n refers to the contour number (see Figs. 5,7,9,11B).</p>	
<b>Y</b>	Variable in plane from $Y_{(n,0)}$ to $-Y_{(n,0)}$
<b>A<sub>u</sub></b>	<b>A<sub>u</sub></b> is the amplitude of the underlying wave
<b>A<sub>s</sub></b>	<b>A<sub>s</sub></b> is the amplitude of the superimposed wave
<b>B<sub>s</sub>(Y)</b>	<b>B<sub>s</sub></b> is a function which biases the wave amplitude in a defined way, e.g. the amplitude of the wave can be increased near the commissure if so desired.
<b>Composite Curve (Figs. 7 &amp; 9)</b>	
<b>X<sub>c</sub></b>	X coordinate for defining the composite curve. This is derived using <b>X<sub>u</sub></b> and <b>X<sub>s</sub></b>
<b>Y<sub>c</sub></b>	Y coordinate for defining the composite curve. This is derived using <b>X<sub>u</sub></b> and <b>X<sub>s</sub></b>

Open Leaflet position (Fig. 10)	
$X_{open}(Z)$ is defined as an ellipse in the XZ axis in the plane defined in Fig. 2 by cutting plane 3-3. The contours defined in <b>Composite Curve</b> are married to the Open Leaflet position $X_{open}(Z)$ to produce the moulded leaflet <b>P</b> . It is defined using the following constants.	
$E_{oJ}$	Open ellipse major axis
$Z_{oo}$	Open ellipse Z-axis offset
$E_{oo}$	Open ellipse X-axis offset
$E_{oN}$	Open ellipse minor axis
$\theta$	Former taper angle

1  
2

Table 4

1 What is claimed is:

2

3 1. A cardiac valve prosthesis comprising:

4 a frame defining a blood flow axis; and

5 at least two flexible leaflets attached to

6 the frame, the at least two leaflets being

7 configured to be movable from an open to a

8 closed position, the at least two leaflets

9 having a blood inlet side and a blood outlet

10 side, the at least two leaflets being in the

11 closed position when fluid pressure is applied

12 to the outlet side, being in the open position

13 when fluid pressure is applied to the inlet side

14 and being in a neutral position intermediate the

15 open and closed position in the absence of fluid

16 pressure being applied to the leaflets, the at

17 least two leaflets including a first leaflet

18 having a surface contour such that when the

19 first leaflet is in the neutral position an

20 intersection of the first leaflet with at least

21 one plane perpendicular to the blood flow axis

22 forms a first composite wave, the first

23 composite wave being substantially defined by a

24 first wave combined with at least a second wave

25 superimposed over the first wave, the first wave

26 having a first frequency, the second wave having

27 a second frequency, the first frequency being

28 different from the second frequency.

29

30 2. The valve prosthesis of claim 1 wherein the

31 first composite wave is defined by a first wave

1 combined with second and third waves superimposed  
2 over the first wave, the third wave having a third  
3 frequency which is different from the first  
4 frequency.

5

6 3. The valve prosthesis of claim 1 wherein the  
7 first wave is symmetric about a plane parallel to and  
8 intersecting the blood flow axis and bisecting the  
9 first leaflet.

10

11 4. The valve prosthesis of claim 1 wherein the  
12 first wave is asymmetric about a plane parallel to  
13 and intersecting the blood flow axis and bisecting  
14 the first leaflet.

15

16 5. The valve prosthesis of claim 1 wherein the  
17 second wave is symmetric about a plane parallel to  
18 and intersecting the blood flow axis and bisecting  
19 the first leaflet.

20

21 6. The valve prosthesis of claim 1 wherein the  
22 second wave is asymmetric about a plane parallel to  
23 and intersecting the blood flow axis and bisecting  
24 the first leaflet.

25

26 7. The valve prosthesis of claim 3 wherein the  
27 second wave is symmetric about a plane parallel to  
28 and intersecting the blood flow axis and bisecting  
29 the first leaflet.

30

1 8. The valve prosthesis of claim 3 wherein the  
2 second wave is asymmetric about a plane parallel to  
3 and intersecting the blood flow axis and bisecting  
4 the first leaflet.

5

6 9. The valve prosthesis of claim 4 wherein the  
7 second wave is symmetric about a plane parallel to  
8 and intersecting the blood flow axis and bisecting.  
9 the first leaflet.

10

11 10. The valve prosthesis of claim 4 wherein the  
12 second wave is asymmetric about a plane parallel to  
13 and intersecting the blood flow axis and bisecting  
14 the first leaflet.

15

16 11. The valve prosthesis of claim 1 wherein the  
17 first composite wave is symmetric about a plane  
18 parallel to and intersecting the blood flow axis and  
19 bisecting the first leaflet.

20

21 12. The valve prosthesis of claim 1 wherein the  
22 composite wave is asymmetric about a plane parallel  
23 to and intersecting the blood flow axis and bisecting  
24 the first leaflet.

25

26 13. The valve prosthesis of claim 1 wherein the at  
27 least two leaflets further include second and third  
28 leaflets and wherein an intersection of the second  
29 and third leaflets with the plane perpendicular to  
30 the blood flow axis forms second and third composite  
31 waves, respectively, the second and third composite

1 waves being substantially the same as the first  
2 composite wave.

3

4 14. The valve prosthesis of claim 1 wherein the  
5 first wave is defined by an equation which is one of  
6 trigonometric, elliptical, hyperbolic, parabolic,  
7 circular, a smooth analytic function and a table of  
8 values.

9

10 15. The valve prosthesis of claim 1 wherein the  
11 second wave is defined by an equation which is one of  
12 trigonometric, elliptical, hyperbolic, parabolic,  
13 circular, a smooth analytic function and a table of  
14 values.

15

16 16. The valve prosthesis of claim 1 wherein the at  
17 least two leaflets are configured such that they are  
18 substantially free of bending stresses when in the  
19 neutral position.

20

21 17. The valve prosthesis of claim 1 wherein the  
22 frame is substantially cylindrical having first and  
23 second ends, one of the ends defining at least two  
24 scalloped edge positions separated by at least two  
25 posts, each post having a tip, and wherein each  
26 leaflet has a fixed edge joined to a respective  
27 scalloped edge portion of the frame and a free edge  
28 extending substantially between the tips of the at  
29 least two posts.

30

1 18. The valve prosthesis of claim 11 wherein the  
2 first and second waves are symmetric about a plane  
3 parallel to and intersecting the blood flow axis and  
4 bisecting the first leaflet.

5

6 19. The valve prosthesis of claim 12 wherein at  
7 least one of the first and second waves is asymmetric  
8 about a plane parallel to and intersecting the blood  
9 flow axis and bisecting the first leaflet.

10

11 20. The valve prosthesis of claim 1 wherein the  
12 first leaflet has a surface contour such that when  
13 the first leaflet is in the neutral position an  
14 intersection of the first leaflet with a plane  
15 parallel to and intersecting the blood flow axis and  
16 bisecting the first leaflet forms a fourth wave.

17

18 21. A method of making a cardiac valve prosthesis  
19 which includes a frame defining a blood flow axis  
20 substantially parallel to the flow of blood through  
21 the valve prosthesis and at least two flexible  
22 leaflets attached to the frame, the method  
23 comprising:

24 providing a forming element having at least  
25 two leaflet forming surfaces;

26 engaging the forming element to the frame;

27 applying a coating over the frame and

28 engaged forming element, the coating binding to

29 the frame, the coating over the leaflet forming

30 surfaces forming the at least two flexible

31 leaflets, the at least two leaflets being



56.

1        configured to be movable from an open to a  
2        closed position, the at least two leaflets  
3        having a blood inlet side and a blood outlet  
4        side, the at least two leaflets being in the  
5        closed position when fluid pressure is applied  
6        to the outlet side, being in the open position  
7        when fluid pressure is applied to the inlet side  
8        and being in a neutral position intermediate the  
9        open and closed position in the absence of fluid  
10       pressure being applied to the leaflets, the at  
11       least two leaflets including a first leaflet  
12       having a surface contour such that when the  
13       first leaflet is in the neutral position an  
14       intersection of the first leaflet with at least  
15       one plane perpendicular to the blood flow axis  
16       forms a first composite wave, the first  
17       composite wave being substantially defined by a  
18       first wave combined with at least a second  
19       superimposed wave, the first wave having a first  
20       frequency, the second wave having a second  
21       frequency, the first frequency being different  
22       from the second frequency; and  
23              disengaging the forming element from the  
24       frame.

25  
26    22. The method of claim 21 wherein the first  
27    composite wave formed in the coating step is defined  
28    by a first wave combined with second and third waves  
29    superimposed over the first wave, the third wave  
30    having a third frequency which is different from the  
31    first frequency.

1

2 23. The method of claim 21 wherein the first wave  
3 formed in the coating step is symmetric about a plane  
4 parallel to and intersecting the blood flow axis and  
5 bisecting the first leaflet.

6

7 24. The method of claim 21 wherein the first wave  
8 formed in the coating step is asymmetric about a  
9 plane parallel to and intersecting the blood flow  
10 axis and bisecting the first leaflet.

11

12 25. The method of claim 21 wherein the second wave  
13 formed in the coating step is symmetric about a plane  
14 parallel to and intersecting the blood flow axis and  
15 bisecting the first leaflet.

16

17 26. The method of claim 21 wherein the second wave  
18 formed in the coating step is asymmetric about a  
19 plane parallel to and intersecting the blood flow  
20 axis and bisecting the first leaflet.

21

22 27. The method of claim 23 wherein the second wave  
23 formed in the coating step is symmetric about a plane  
24 parallel to and intersecting the blood flow axis and  
25 bisecting the first leaflet.

26

27 28. The method of claim 23 wherein the second wave  
28 formed in the coating step is asymmetric about a  
29 plane parallel to and intersecting the blood flow  
30 axis and bisecting the first leaflet.

31

1 29. The method of claim 24 wherein the second wave  
2 formed in the coating step is symmetric about a plane  
3 parallel to and intersecting the blood flow axis and  
4 bisecting the first leaflet.

5

6 30. The method of claim 24 wherein the second wave  
7 formed in the coating step is asymmetric about a  
8 plane parallel to and intersecting the blood flow  
9 axis and bisecting the first leaflet.

10

11 31. The method of claim 21 wherein the first  
12 composite wave formed in the coating step is  
13 symmetric about a plane parallel to and intersecting  
14 the blood flow axis and bisecting the first leaflet.

15

16 32. The method of claim 21 wherein the first  
17 composite wave formed in the coating step is  
18 asymmetric about a plane parallel to and intersecting  
19 the blood flow axis and bisecting the first leaflet.

20

21 33. The method of claim 21 wherein the at least two  
22 leaflets formed in the coating step include second  
23 and third leaflets and wherein an intersection of the  
24 second and third leaflets with the plane  
25 perpendicular to the blood flow axis forms second and  
26 third composite waves, respectively, the second and  
27 third composite waves being substantially the same as  
28 the first composite wave.

29

30 34. The method of claim 21 wherein the first wave  
31 formed in the coating step is defined by an equation

1 which is one of trigonometric, elliptical,  
2 hyperbolic, parabolic, circular, a smooth analytic  
3 function and a table of values.

4

5 35. The method of claim 21 wherein the second wave  
6 formed in the coating step is defined by an equation  
7 which is one of trigonometric, elliptical,  
8 hyperbolic, parabolic, circular, a smooth analytic  
9 function and a table of values.

10

11 36. The method of claim 31 wherein the first and  
12 second waves formed in the coating step are symmetric  
13 about a plane parallel to and intersecting the blood  
14 flow axis and bisecting the first leaflet.

15

16 37. The method of claim 32 wherein at least one of  
17 the first and second waves formed in the coating step  
18 is asymmetric about a plane parallel to and  
19 intersecting the blood flow axis and bisecting the  
20 first leaflet.

21

22 38. The method of claim 21 wherein the at least two  
23 leaflets formed in the coating step are configured  
24 such that they are substantially free of bending  
25 stresses when in the neutral position.

26

27 39. A cardiac valve prosthesis comprising:  
28 a frame defining a blood flow axis; and  
29 at least two leaflets attached to the frame  
30 including a first leaflet having an internal  
31 surface facing the blood flow axis and an

1 external surface facing away from the blood flow  
2 axis, the first leaflet being configured such  
3 that a mean thickness of a first half of the  
4 first leaflet is different than a mean thickness  
5 of a second half of the first leaflet, the first  
6 and second halves being defined by a plane  
7 parallel to and intersecting the blood flow axis  
8 and bisecting the first leaflet.

9  
10 40. The cardiac valve prosthesis of claim 39 wherein  
11 the first leaflet is further configured such that a  
12 thickness of the first leaflet between the internal  
13 and external surfaces along a cross section defined  
14 by the intersection of a plane perpendicular to the  
15 blood flow axis and the first leaflet increases  
16 gradually and substantially continuously from a first  
17 end of the cross section to a second end of the cross  
18 section.

19  
20 41. A method of making a cardiac valve prosthesis  
21 which includes a frame defining a blood flow axis  
22 substantially parallel to the flow of blood through  
23 the valve prosthesis and at least two flexible  
24 leaflets attached to the frame, the method  
25 comprising:

26 providing a mould having a cavity sized to  
27 accommodate the frame;  
28 inserting the frame into the mould;  
29 inserting the mould into an injection  
30 moulding machine;

1           injecting molten polymer into the cavity of  
2           the mould to form the at least two leaflets and  
3           bond the at least two leaflets to the frame, the  
4           cavity being shaped to form the at least two  
5           leaflets in a desired configuration, the at  
6           least two leaflets being configured to be  
7           movable from an open to a closed position, the  
8           at least two leaflets having a blood inlet side  
9           and a blood outlet side, the at least two  
10          leaflets being in the closed position when fluid  
11          pressure is applied to the outlet side, being in  
12          the open position when fluid pressure is applied  
13          to the inlet side and being in a neutral  
14          position intermediate the open and closed  
15          position in the absence of fluid pressure being  
16          applied to the leaflets, the at least two  
17          leaflets including a first leaflet having a  
18          surface contour such that when the first leaflet  
19          is in the neutral position an intersection of  
20          the first leaflet with at least one plane  
21          perpendicular to the blood flow axis forms a  
22          first composite wave, the first composite wave  
23          being substantially defined by a first wave  
24          combined with at least a second superimposed  
25          wave, the first wave having a first frequency,  
26          the second wave having a second frequency, the  
27          first frequency being different from the second  
28          frequency.

29

30   42. The method of claim 41 wherein the first  
31   composite wave formed in the injecting step is

1 defined by a first wave combined with second and  
2 third waves superimposed over the first wave, the  
3 third wave having a third frequency which is  
4 different from the first frequency.

5

6 43. The method of claim 41 wherein the first wave  
7 formed in the injecting step is symmetric about a  
8 plane parallel to and intersecting the blood flow  
9 axis and bisecting the first leaflet.

10

11 44. The method of claim 41 wherein the first wave  
12 formed in the injecting step is asymmetric about a  
13 plane parallel to and intersecting the blood flow  
14 axis and bisecting the first leaflet.

15

16 45. The method of claim 41 wherein the second wave  
17 formed in the injecting step is symmetric about a  
18 plane parallel to and intersecting the blood flow  
19 axis and bisecting the first leaflet.

20

21 46. The method of claim 41 wherein the second wave  
22 formed in the injecting step is asymmetric about a  
23 plane parallel to and intersecting the blood flow  
24 axis and bisecting the first leaflet.

25

26 47. The method of claim 43 wherein the second wave  
27 formed in the injecting step is symmetric about a  
28 plane parallel to and intersecting the blood flow  
29 axis and bisecting the first leaflet.

30

1 48. The method of claim 43 wherein the second wave  
2 formed in the injecting step is asymmetric about a  
3 plane parallel to and intersecting the blood flow  
4 axis and bisecting the first leaflet.

5

6 49. The method of claim 44 wherein the second wave  
7 formed in the injecting step is symmetric about a  
8 plane parallel to and intersecting the blood flow  
9 axis and bisecting the first leaflet.

10

11 50. The method of claim 44 wherein the second wave  
12 formed in the injecting step is asymmetric about a  
13 plane parallel to and intersecting the blood flow  
14 axis and bisecting the first leaflet.

15

16 51. The method of claim 41 wherein the first  
17 composite wave formed in the injecting step is  
18 asymmetric about a plane parallel to and intersecting  
19 the blood flow axis and bisecting the first leaflet.

20

21 52. The method of claim 41 wherein the first  
22 composite wave formed in the injecting step is  
23 asymmetric about a plane parallel to and intersecting  
24 the blood flow axis and bisecting the first leaflet.

25

26 53. The method of claim 41 wherein the at least two  
27 leaflets formed in the injecting step include second  
28 and third leaflets and wherein an intersection of the  
29 second and third leaflets with the plane  
30 perpendicular to the blood flow axis forms second and  
31 third composite waves, respectively, the second and



1 third composite waves being substantially the same as  
2 the first composite wave.

3

4 54. The method of claim 41 wherein the first wave  
5 formed in the injecting step is defined by an  
6 equation which is one of trigonometric, elliptical,  
7 hyperbolic, parabolic, circular, a smooth analytic  
8 function and a table of values.

9

10 55. The method of claim 41 wherein the second wave  
11 formed in the injecting step is defined by an  
12 equation which is one of trigonometric, elliptical,  
13 hyperbolic, parabolic, circular, a smooth analytic  
14 function and a table of values.

15

16 56. The method of claim 51 wherein the first and  
17 second waves formed in the injecting step are  
18 symmetric about a plane parallel to and intersecting  
19 the blood flow axis and bisecting the first leaflet.

20

21 57. The method of claim 52 wherein at least one of  
22 the first and second waves formed in the injecting  
23 step is asymmetric about a plane parallel to and  
24 intersecting the blood flow axis and bisecting the  
25 first leaflet.

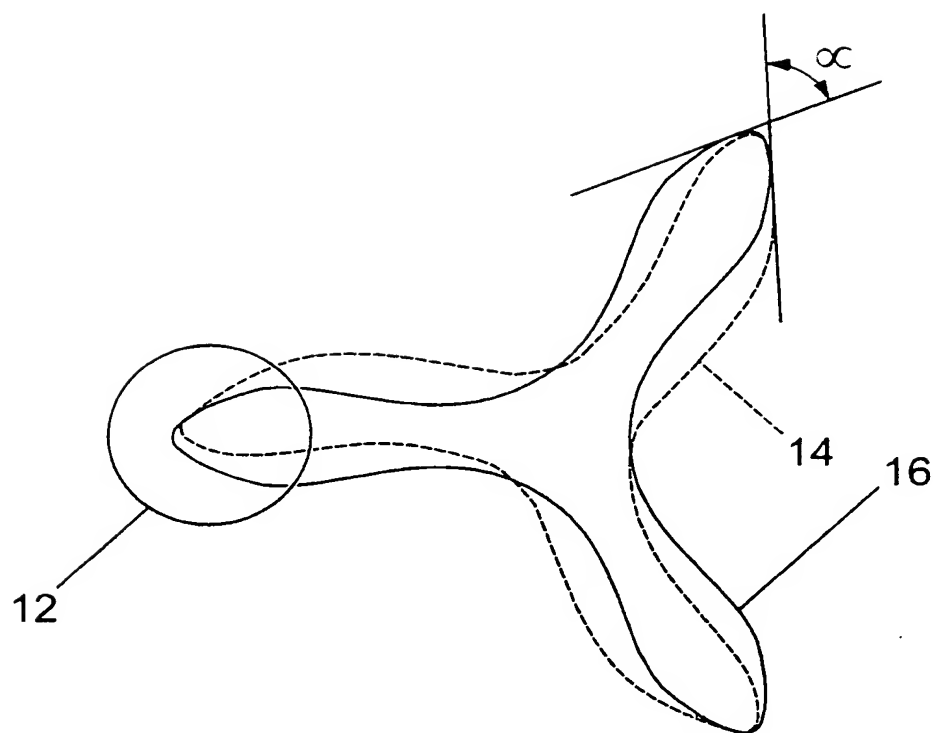
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27 58. The method of claim 41 wherein the at least two  
28 leaflets formed in the injecting step are configured  
29 such that they are substantially free of bending  
30 stresses when in the neutral position.

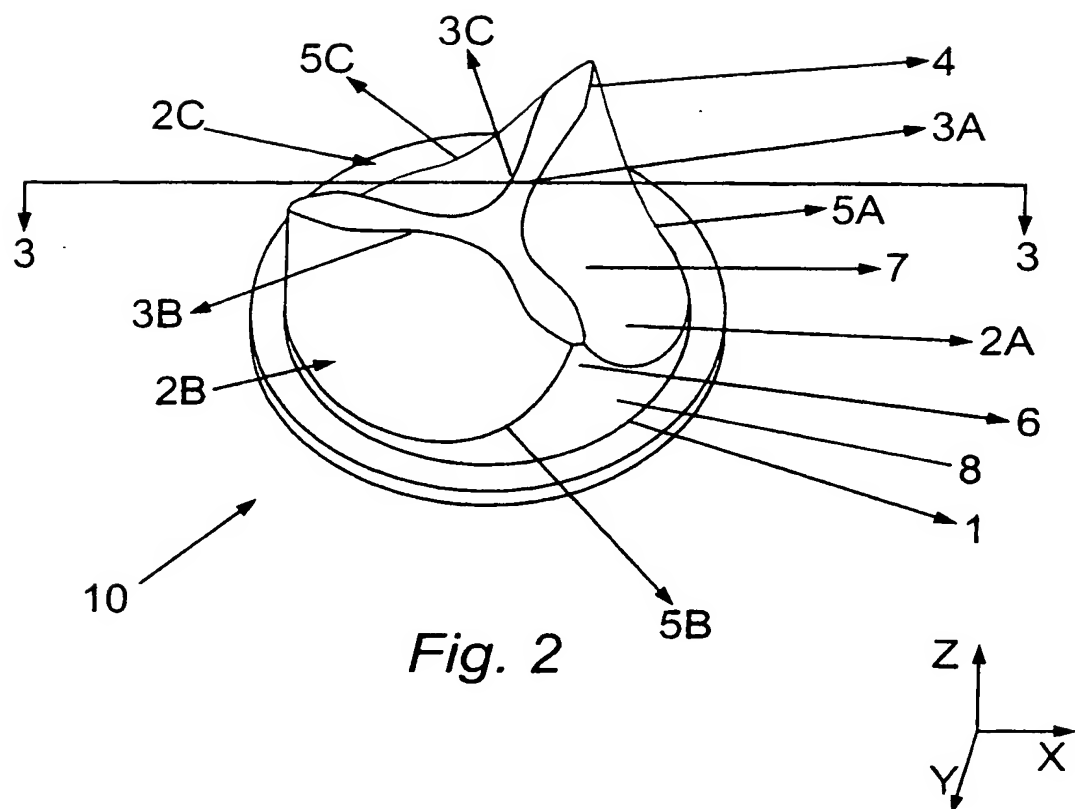
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- 1 59. A method of designing a cardiac valve prosthesis  
2 which includes a frame and at least two flexible  
3 leaflets attached to the frame, the method  
4 comprising:  
5           defining a first desired shape of the  
6       leaflets in a first position;  
7           defining a second desired shape of the  
8       leaflets in a second position different from the  
9       first position; and  
10          conducting a draping analysis to identify  
11       values of adjustable parameters defining at  
12       least one of the first and second shapes to  
13       ensure that the leaflets are comprised of a  
14       sufficient amount and distribution of material  
15       for the leaflets to assume both the first and  
16       second desired shapes.  
17
- 18 60. The method of claim 59 wherein at least one of  
19 the first and second positions formed in the defining  
20 steps is a closed position and the other of the first  
21 and second positions is a partially open position.

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*Fig. 1*

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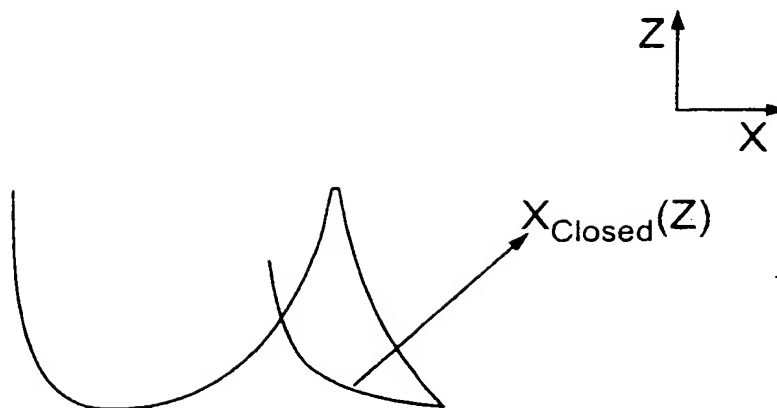


Fig. 3

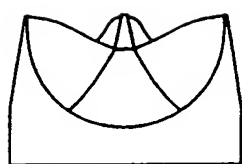


Fig. 4A

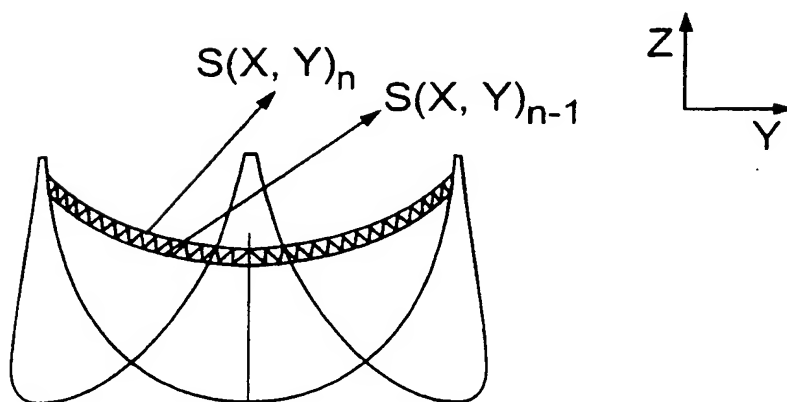


Fig. 4B

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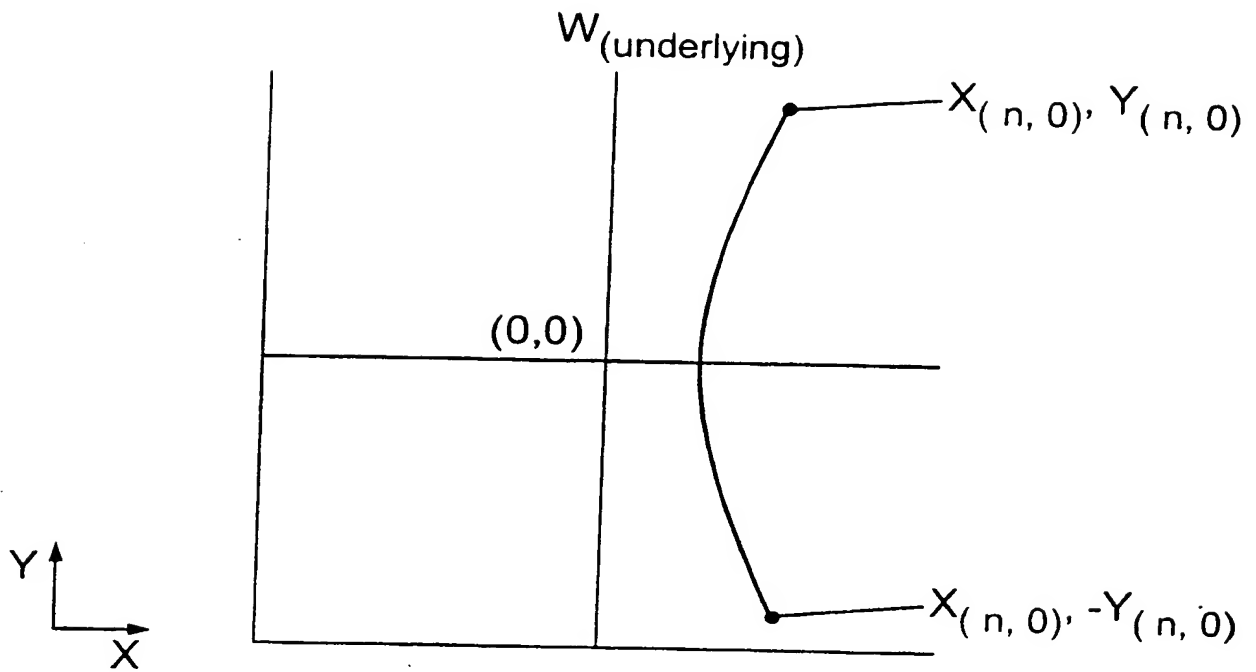


Fig. 5

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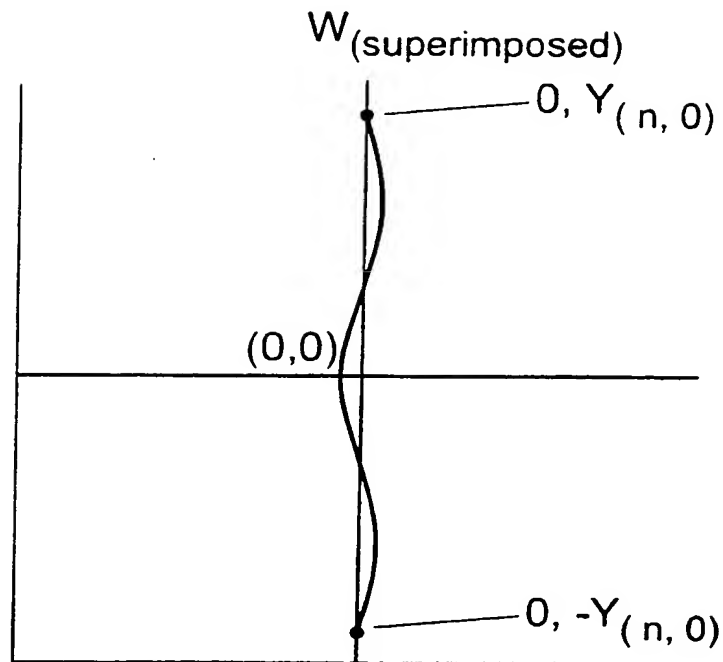


Fig. 6

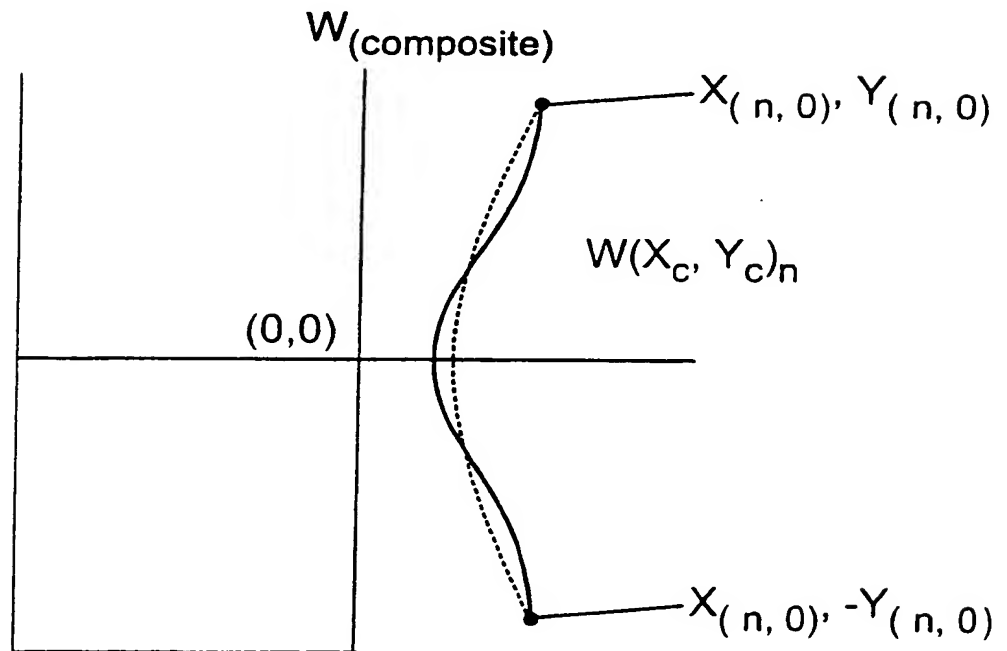


Fig. 7

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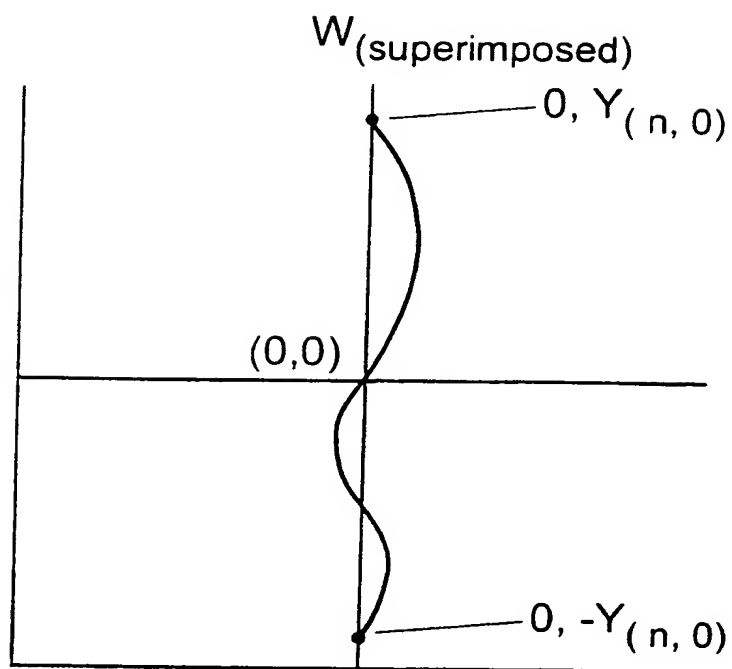


Fig. 8

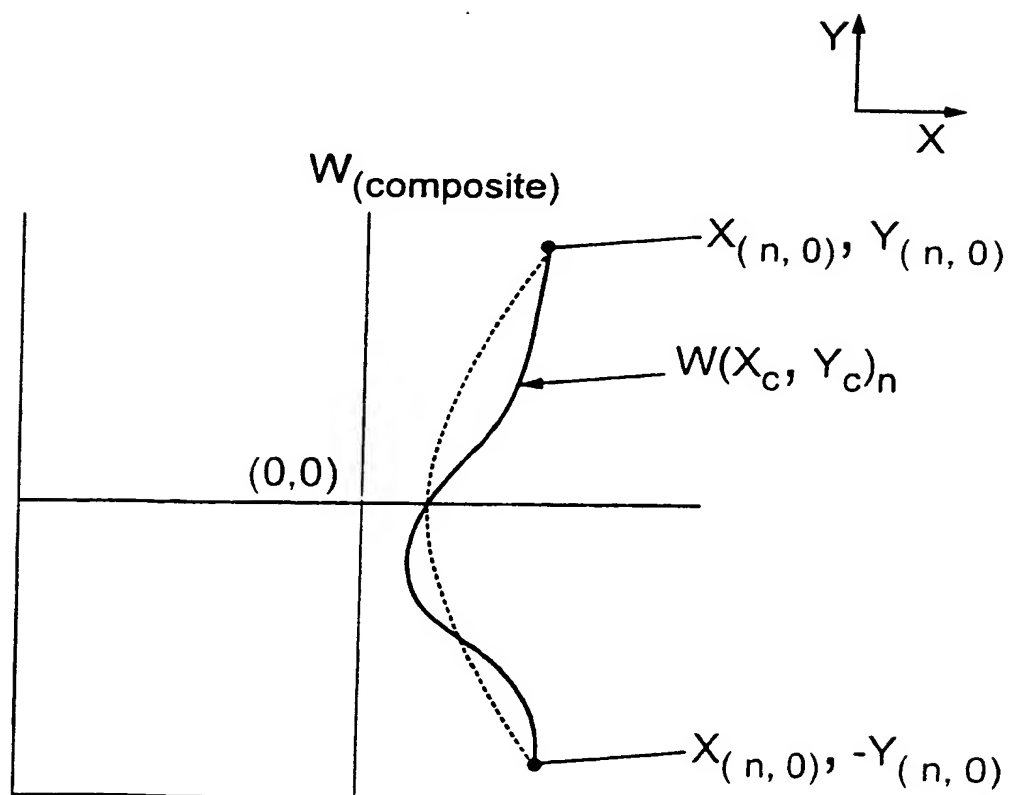


Fig. 9



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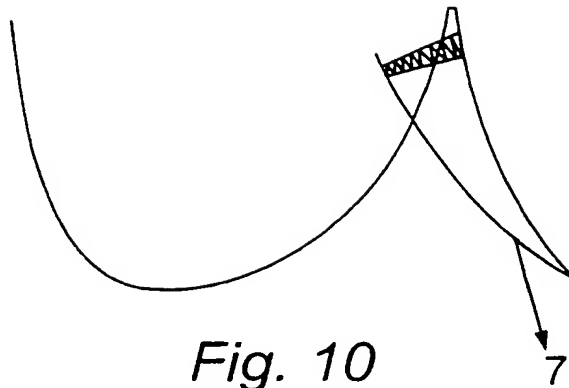


Fig. 10

Fig. 11A

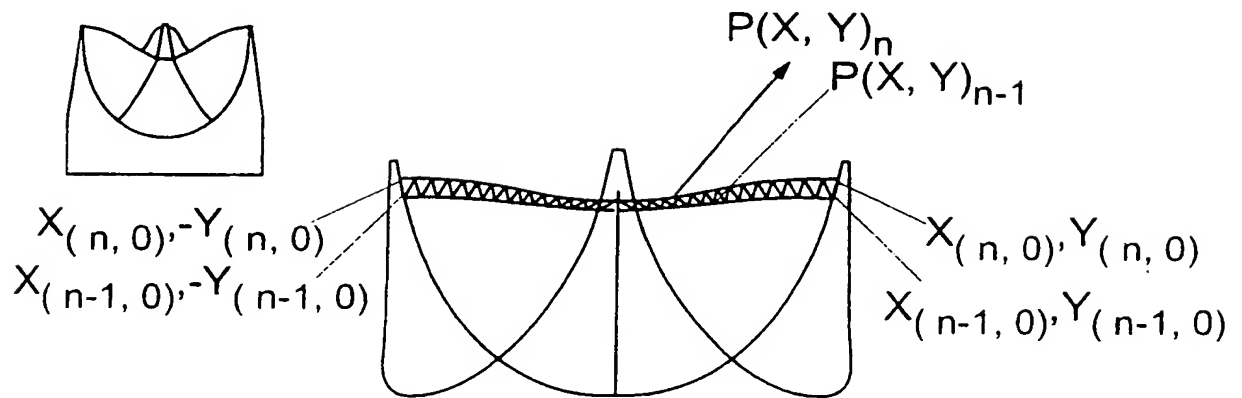
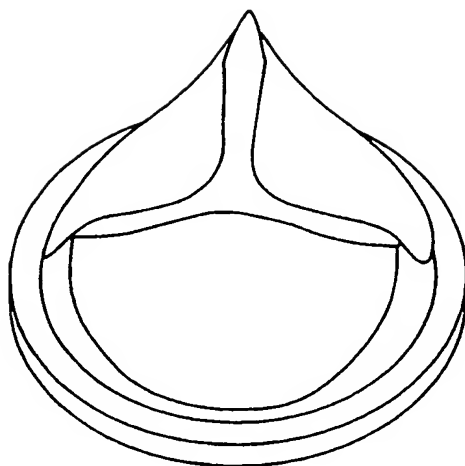
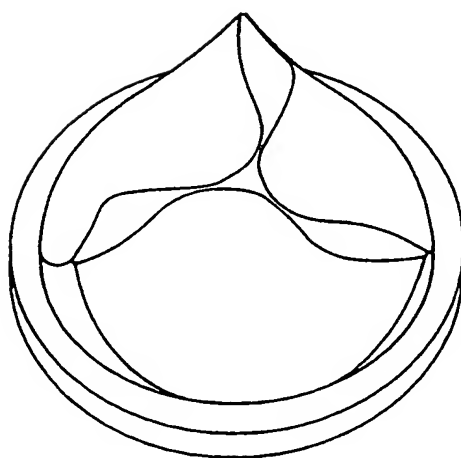


Fig. 11B

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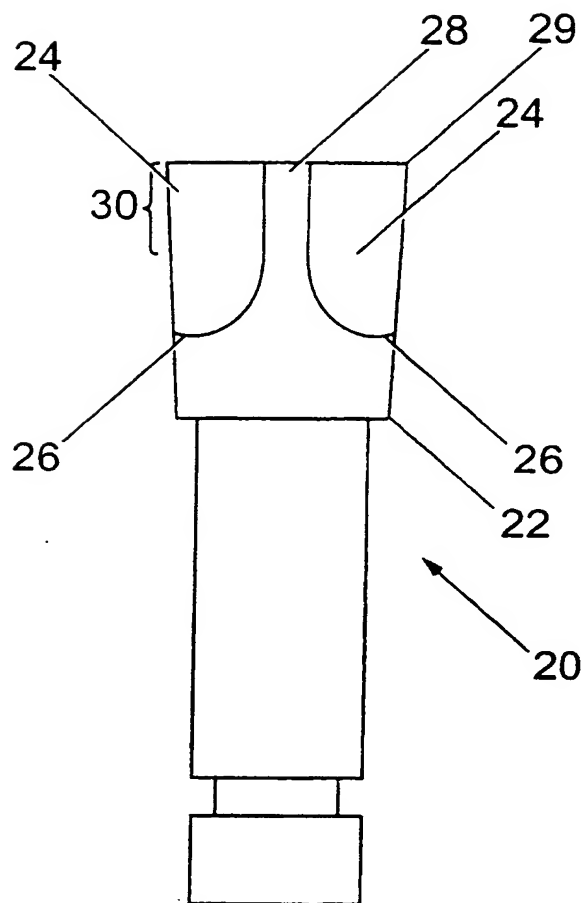


*Fig. 12*



*Fig. 13*

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*Fig. 14*

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/04673

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61F2/24

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 562 729 A (PURDY DAVID L ET AL) 8 October 1996 (1996-10-08) figure 38 column 11, line 22 - line 47 column 11, line 56 - column 12, line 63 column 13, line 6 - line 45	1, 21, 41, 59, 60
A	---	39
X	US 5 800 527 A (JANSEN ULRICH ET AL) 1 September 1998 (1998-09-01) figures 5-8 column 8, line 50 - column 9, line 31	1
A	---	21, 39, 41, 59
	--- -/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

28 March 2001

Date of mailing of the international search report

04/04/2001

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# INTERNATIONAL SEARCH REPORT

Inter. Application No

PCT/GB 00/04673

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	----	21
A	US 5 358 518 A (CAMILLI SANTE) 25 October 1994 (1994-10-25) figures 1A,2A,3A,4A column 1, line 50 -column 2, line 61 -----	1,21,39, 41,59

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Information on patent family members

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